POWER OF PROVIDERS

Peer to Peer knowledge sharing webinar series

Washington State Department of HEALTH

Obtaining Continuing Education

- Continuing education is available for physicians (MD, DO, ND), physician assistants, nurses (RN, ARNP, LPN), and medical assistants.
- Successful completion of this continuing education activity includes the following:
  - Attending the entire live webinar or watching the webinar recording
  - Complete the evaluation after the live webinar or webinar recording
  - **On the evaluation, please check Yes if you're interested in contact hours and please specify which type of continuing education you wish to obtain**
- **Please note:** CE certificates are NOT generated after evaluation completion—CE certificates will be sent by DOH within a few weeks after evaluation completion
- Expiration date is 6/29/2024.

Continuing Medical Education

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Federation of State Medical Boards, Washington Medical Commission and the Washington State Department of Health. The Federation of State Medical Boards is accredited by the ACCME to provide continuing medical education for physicians.

The Federation of State Medical Boards designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Continuing Education

- This nursing continuing professional development activity was approved by Montana Nurses Association, an accredited approver with distinction by the American Nurses Credentialing Center's Commission on Accreditation. Upon successful completion of this activity, 1.0 contact hours will be awarded.

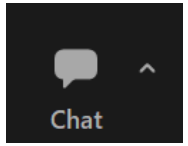
- This program has been granted prior approval by the American Association of Medical Assistants (AAMA) for 1.0 administrative continuing education unit.

Disclosures

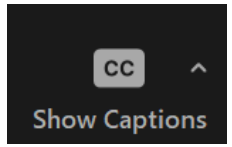
Dr Helen Chu receives research support from Gates Ventures, NIH, CDC, Gates Foundation, DARPA, Sanofi-Pasteur, Cepheid and serves on advisory boards for Abbvie, Merck, Pfizer, Ellume, and the Gates Foundation.

Dr Helen Chu has served as a co-investigator on studies funded by Pfizer, Novavax, and Glaxo Smith Kline.

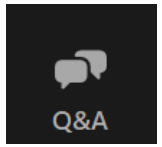
Zoom Housekeeping



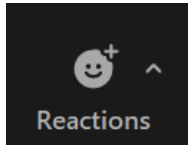
- Team shares information here
- Use for audience participation



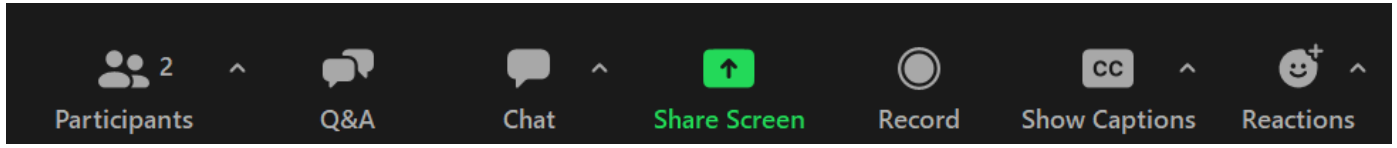
- Click to enable automatic closed captions



- Submit questions to presenter and team



- Click top-right arrow to hide participant reactions



About the Power of Providers Initiative

- Support and equip health care providers to serve as trusted sources of COVID-19 vaccine information for their patients and their communities
- Respond to member requests for resources
- Work together to increase vaccine rates across the state

Who can join POP?

Current Membership

- 4,500+ individuals
- 400 health care organizations
- 90 different health care roles
- Over 20 partnering health care associations

Any health care provider who engages with the people they serve about COVID-19 vaccinations is eligible—the ability to educate and refer is as important as administering the vaccine!

Visit our website to learn more at doh.wa.gov/joinpop. Fill out the member signup form to join the initiative.

Current Resources

POP Shop

- Webpage to order free patient handouts, posters, discussion guides, other materials

doh.wa.gov/form/pop-shop

Biweekly e-newsletter

- New resources, timely and relevant updates for members
- Featuring POP member stories in Provider Spotlights

POP en Español

- Updates, links, fact sheets, other resources for providers serving Spanish-speaking populations

doh.wa.gov/popesp

Current Opportunities

Provider Advisory Group

- Multi-disciplinary group of POP members who inform and help guide our work

Peer-to-Peer webinars

- Learn about topics related to COVID vaccine from speakers who work in health care
- To learn about upcoming topics, register, and view recordings, visit doh.wa.gov/pop

Member engagement

- POP staff are available and engaged in conversations with providers across the state to learn about your experiences, challenges, and feedback for DOH

Peer-to-Peer Webinars

- Health care providers share expertise and knowledge with one another
- DOH provides meeting space only, not content

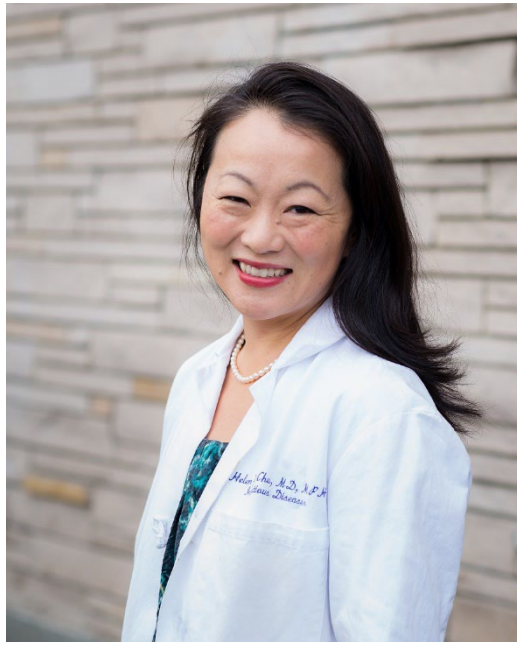
Effectively Engaging Communities series with **Dr Michelle Andrasik**:

- April 19: Building Relationships and Establishing Trust
- May 10: Addressing Vaccine Hesitancy

Today's Presenter

Dr Helen Chu MD, MPH

- Professor of Medicine at the University of Washington.
- Earned her M.D. at Duke and her M.P.H at UW.
- Research focus is on preventive interventions against influenza, RSV and emerging respiratory viruses, including SARS-CoV-2. She was a Multiple Principal Investigator of the Seattle Flu Study, which first identified COVID-19 community transmission in the United
- Interested in defining clinical and immune correlates of protection against respiratory viruses and describing mechanisms of maternal-fetal immunity against respiratory viruses.



University of Washington Research Updates on Long COVID

Helen Y. Chu, MD MPH
Professor of Medicine
University of Washington
March 29, 2024

Washington State Department of Health
Webinar for Power of Providers

UW Medicine
SCHOOL OF MEDICINE

SCHOOL OF PUBLIC HEALTH
UNIVERSITY of WASHINGTON

Disclosures

I received research support from Gates Ventures, NIH, CDC, Gates Foundation, DARPA, Sanofi-Pasteur, and Cepheid and served on advisory boards for Vir, Abbvie, Merck, Pfizer, Ellume, and the Gates Foundation.

I have served as a co-investigator on studies funded by Pfizer, Novavax, and Glaxo Smith Kline.

These studies were funded by the Gates Foundation and NIH.

Outline

- Definitions, risk factors, and clinical manifestations
- Results from research studies at the University of Washington
- New clinical trials

Terminology

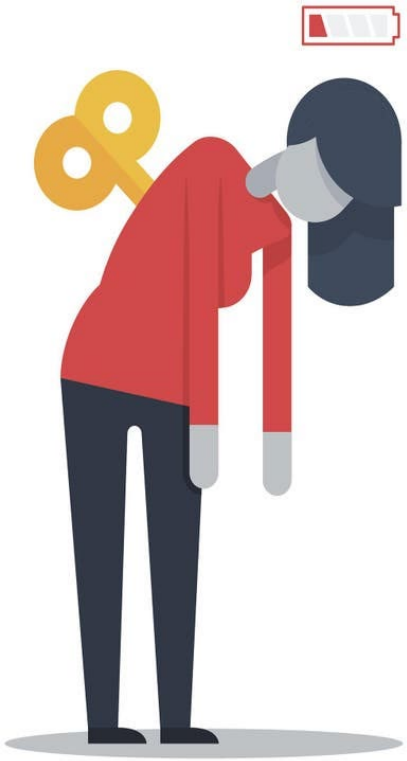
- Different terms
  - NIH: Post-Acute Sequelae of COVID-19 (PASC)
  - CDC: Post-COVID Conditions (PCC)
  - Long COVID
  - Long-haul COVID

- WHO definition: usually three months from the onset of the COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis
- CDC definition: symptoms developing during or after COVID-19 infection, but are present four or more weeks after infection with no alternative diagnosis
- ICD-10: U09.9 – Unspecified Post-COVID Condition

Long COVID Overlaps with Post-Viral Syndromes

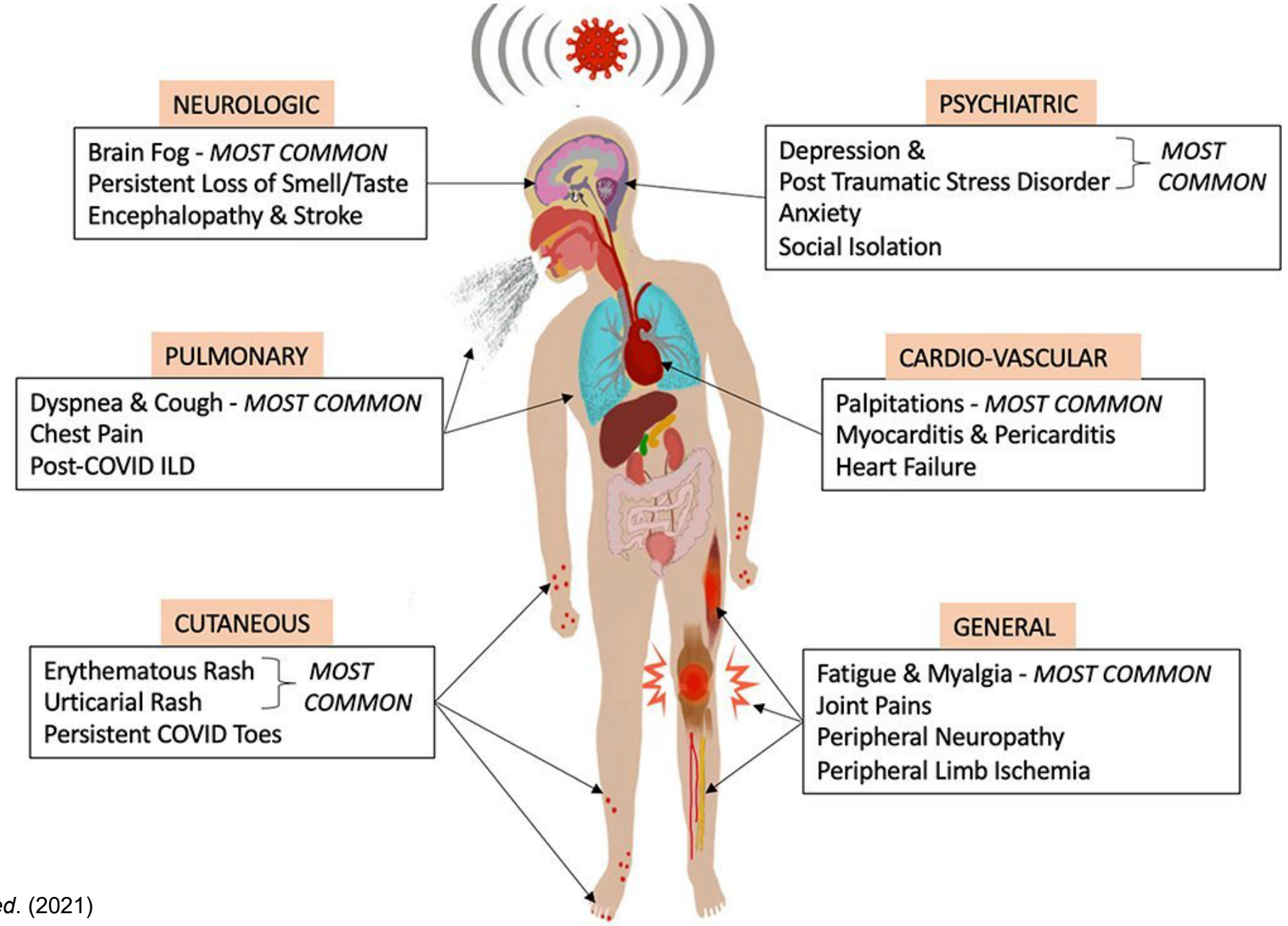
- Ebola, SARS, MERS survivors have similar patterns of persistent symptoms
  - Persistent shortness of breath, fatigue, reduced quality of life and mental health problems after SARS-CoV-1
  - Chronic fatigue in survivors of MERS in 48% at one year
  - Post-Ebola virus syndrome of fatigue, joint and muscle pain (70%), headache (48%), ocular problems (14%)

- Overlap with myalgic encephalomyelitis/chronic fatigue syndrome after viral illnesses like Chikungunya, Lyme or Epstein-Barr virus infection
  - Fatigue and myalgias
  - Problems with memory/concentration

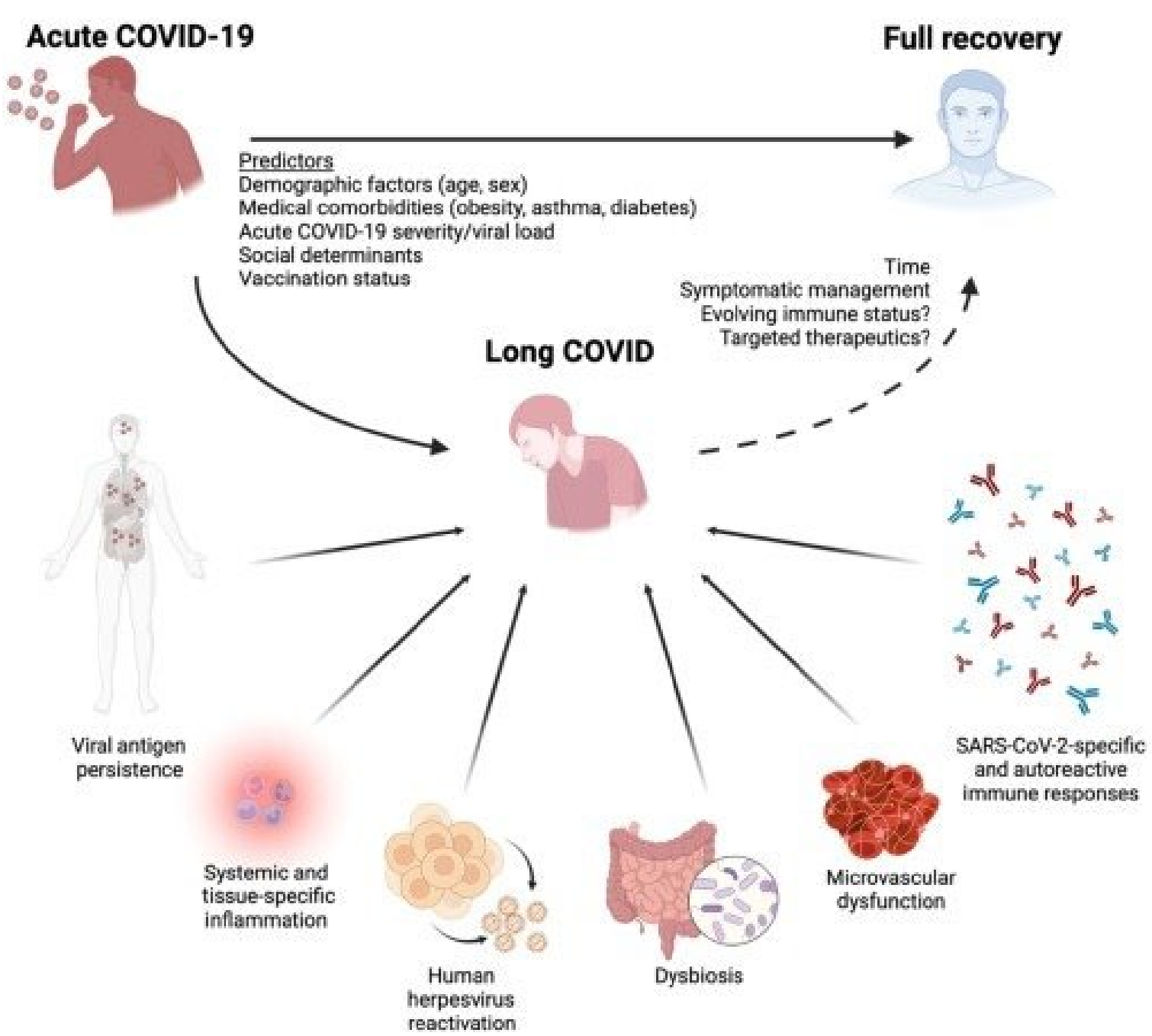


Nalbandian, Nature Medicine 2021
O'Sullivan, Clinical Medicine 2021
Scott, EID 2016

Long COVID is a multi-organ systemic inflammatory disease



Garg M, *Int J Gen Med*. (2021)



Multiple different mechanisms likely account for the different manifestations of long COVID

Peluso & Deeks, Trends Immunology (2022);

Mechanisms of PASC

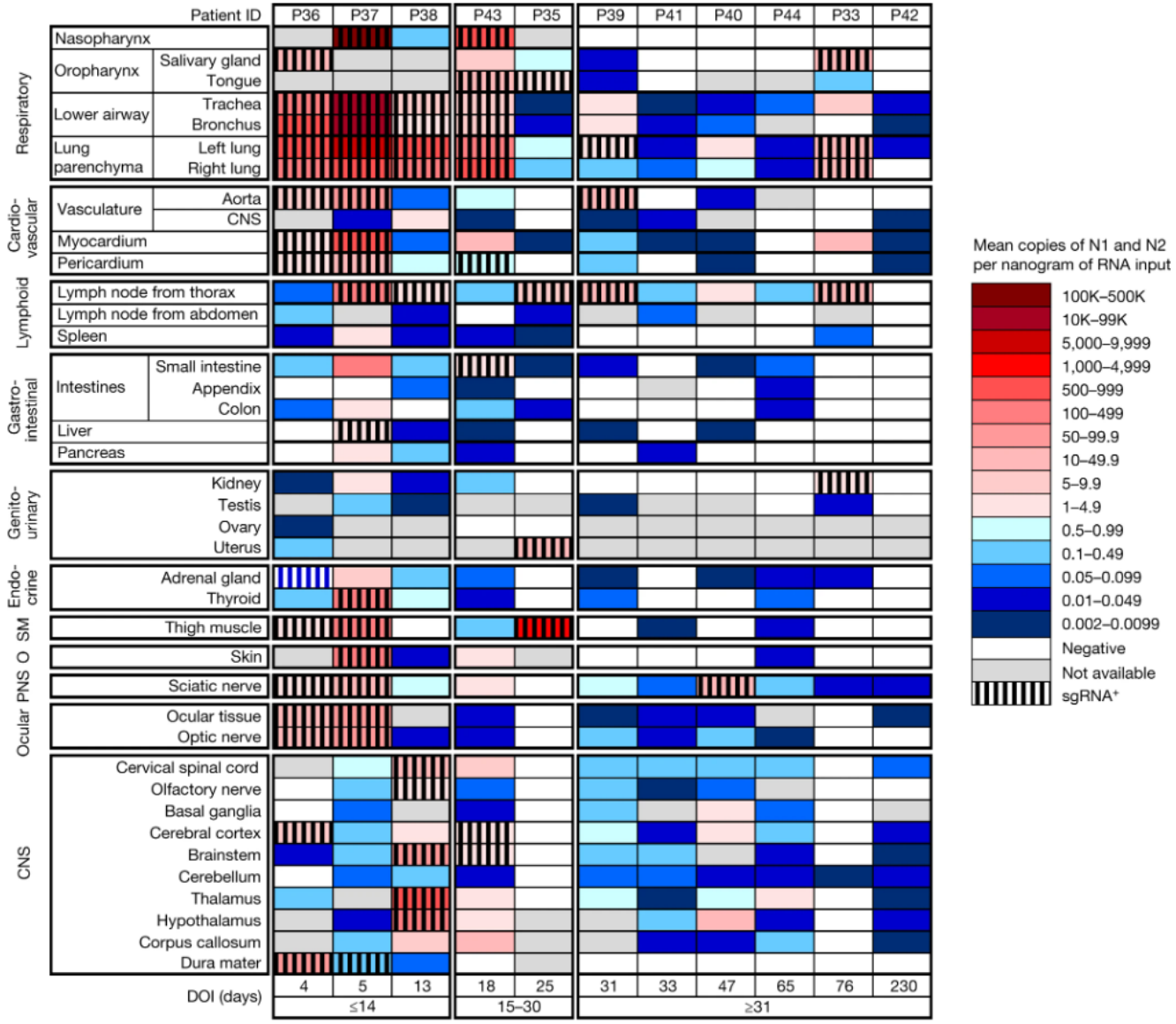
- Viral persistence
  - Reservoir of replicating virus with associated ongoing inflammation
- Cardiopulmonary disease: Virus-specific pathophysiologic changes, microvascular thromboembolism, direct myocardial injury
- Autoimmune disease: Immunologic aberrations & inflammatory damage in response to the acute infection
- Neurologic sequelae
  - Microvascular ischemia & injury, immobility, metabolic alterations during critical illness
  - Mimics post-chemotherapy brain with elevated CSF cytokines, myelin loss

Nalbandian, Nature Medicine, 2021

SARS-CoV-2 Viral Persistence

Distribution, quantification and replication of SARS-COV-2 in autopsy tissues:

- RNA copy number decreases over time from initial infection.
- RNA persists to 230 days
- sgRNA persists to 76 days



Stein SR et al. Nature (2022);
https://doi.org/10.1038/s41586-022-05542-y
Slide courtesy of Jason Goldman, MD, MPH

SARS-CoV-2 Anti-Viral Prevention Strategy

JAMA Internal Medicine

Original Investigation

March 23, 2023

Association of Treatment With Nirmatrelvir and the Risk of Post-COVID-19 Condition

Yan Xie, PhD[1,2]; Taeyoung Choi, MPH[1,2]; Ziyad Al-Aly, MD[1,2,3,4,5]

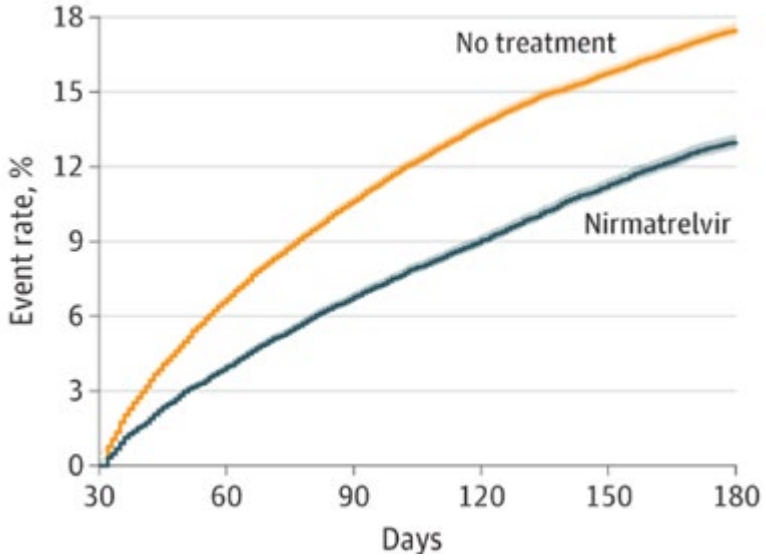
Observational data… in high risk outpatients (>281k veterans)

<u>Paxlovid given at the time of Acute COVID-19 reduces risk of Long Covid:</u>

- Relative Risk of long COVID:

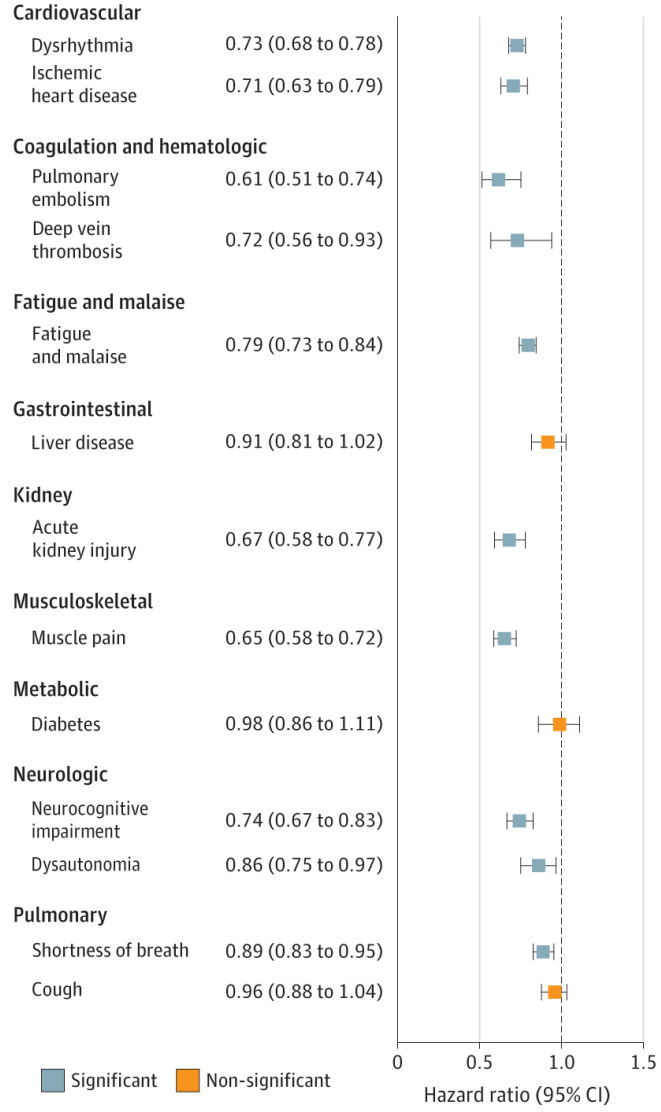
0.74 (95%CI, 0.72-0.77)

Any long COVID



Xie Y et al. JAMA Internal Medcine (2023)
DOI: 10.1001/jamainternmed.2023.0743
Slide courtesy of Jason Goldman, MD, MPH

Components of long COVID



Outline

- Definitions, risk factors, and clinical manifestations

- Results from research studies at the University of Washington

- New clinical trials

January 21, 2020

First Patient With Wuhan Coronavirus Is Identified in the U.S.

A man in Washington State is infected with a new respiratory virus. Federal officials plan to expand screenings for the infection at major airports.

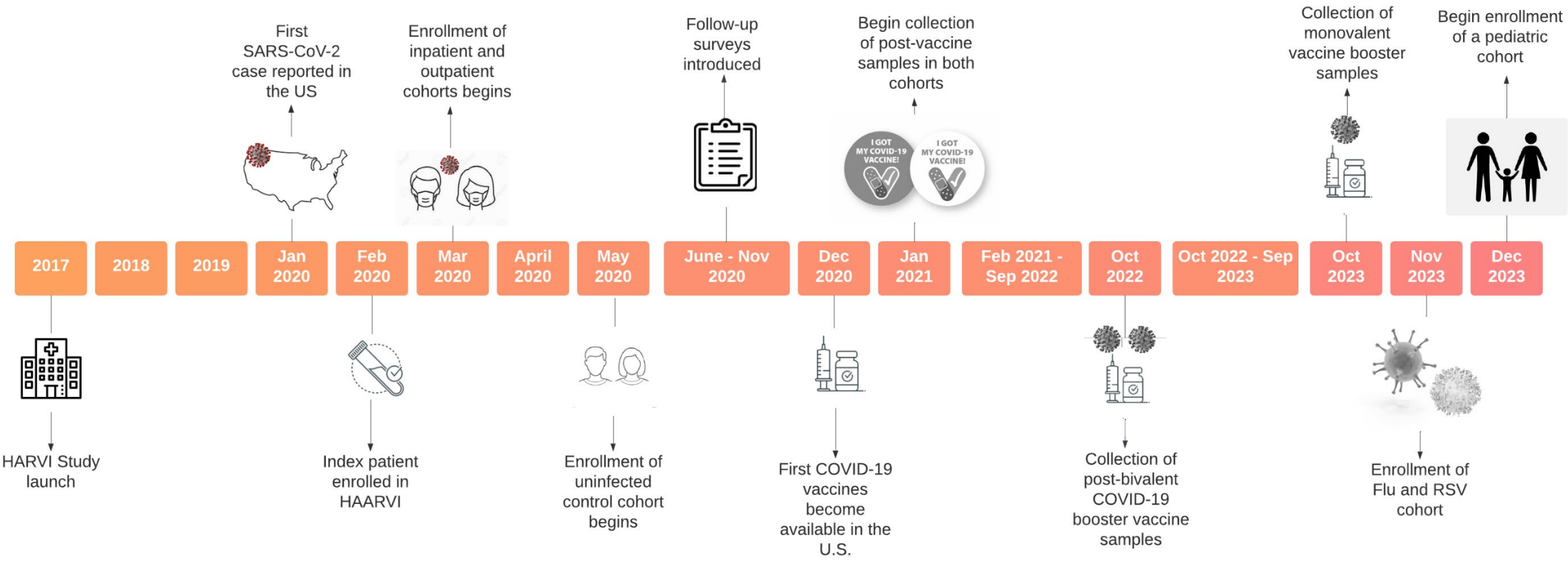
February 2020: UW study established to enroll individuals with COVID-19

- Blood samples from individuals recovered from COVID-19 were critically needed early in the pandemic
  - To see if vaccines can make the same immune response
  - As the source of samples to develop therapies (monoclonal antibodies)
  - To understand how long immunity lasts, and identify early markers of severe disease

- Transfer of human samples across international boundaries is challenging
- Early in a pandemic, research samples were scarce, route of transmission of SARS-CoV-2 was unclear, and heightened infection control precautions were in place
- Seattle, WA was the location of the first U.S. case of COVID-19

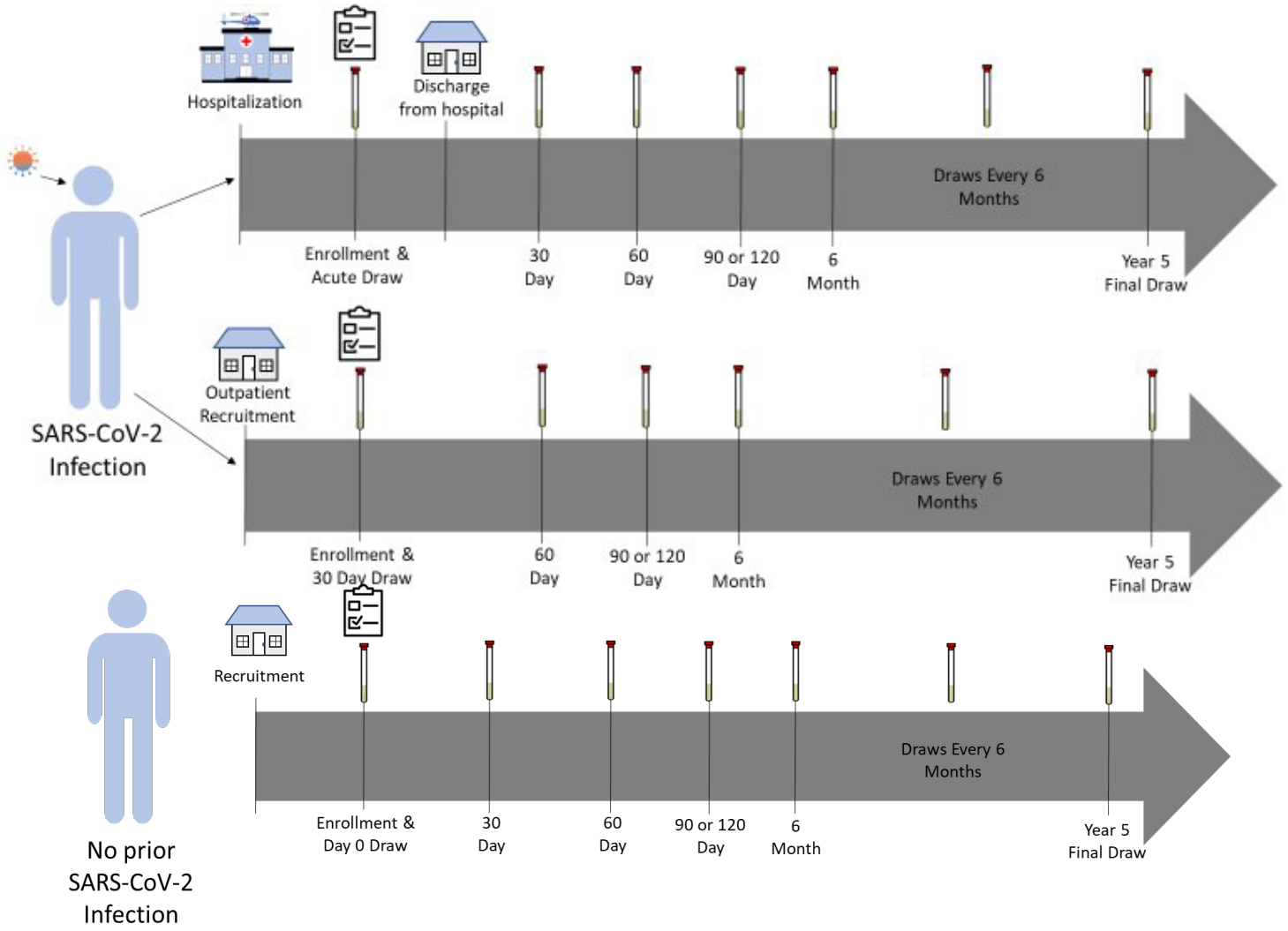
We had an ongoing research study of adults with respiratory viral infections and were able to work with our infection control, human subjects, and environmental health services colleagues to start enrolling individuals with SARS-CoV-2 within days

Study Milestones



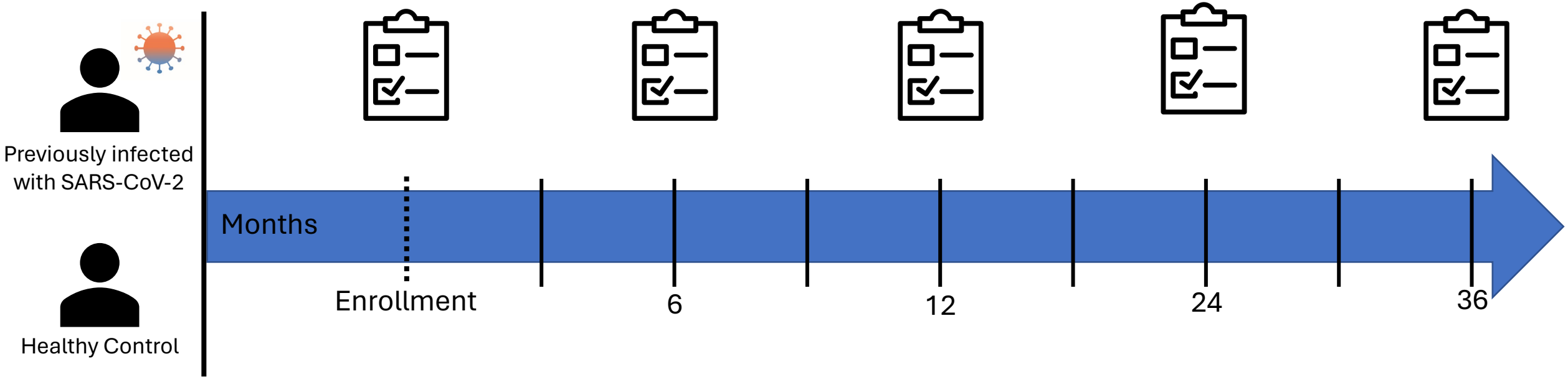
Antibody escape: Greaney, Cell Host Microbe 2021
Comparison of vaccines: Cameroni, Nature 2021, Bowen Science 2022
Hybrid immunity: Rodda, Cell 2022
Omicron antigenic sin: Addetia, Immunity 2024

Enrollment and Follow-up



- Inpatients were enrolled during hospitalization. Loss to follow up in this cohort was significant
- The outpatient cohort was enrolled 30 days after initial infection. Some were hospitalized during their acute illness, but no acute samples were collected
- An uninfected control cohort was concurrently enrolled

Collection of Symptom Data

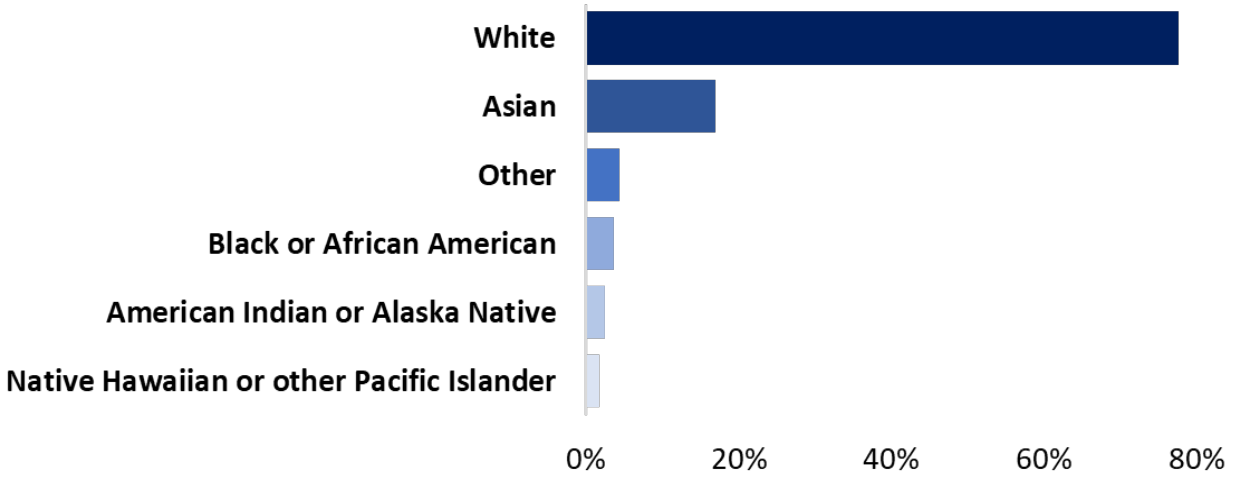


Symptom data is collected at enrollment, and 6-, 12-, 24-, and 36-months post-infection or post-enrollment

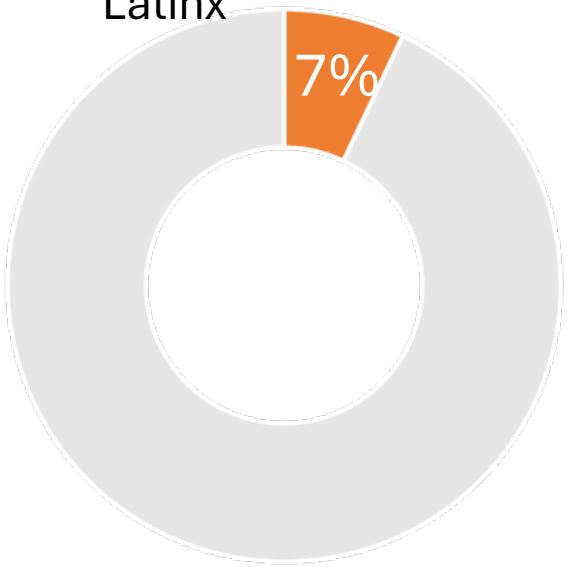
Total Enrollment: 646

Inpatients	Outpatients	Controls
50	489	107

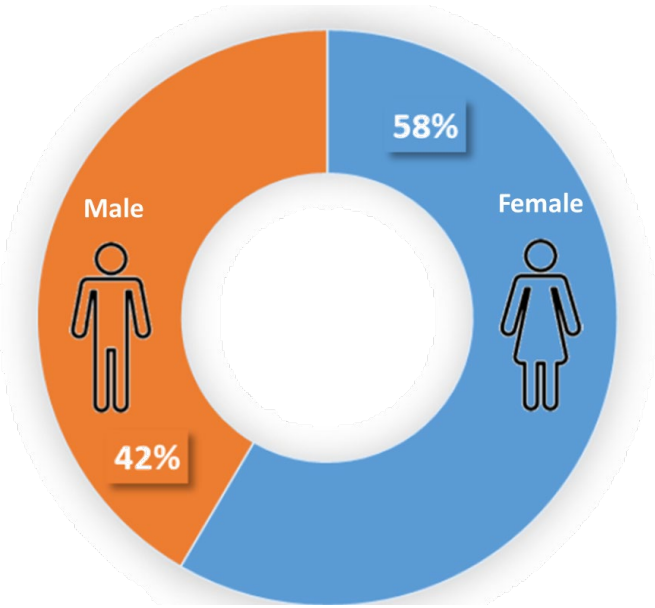
Race



Hispanic or Latinx



Sex



haarvi
Hospitalized or Ambulatory Adults with Respiratory Viral Infections

Professor Jan Englund
Seattle Children's

Enrolling the first US patient with SARS-CoV-2 (no masks!)

- Source of monoclonal antibody (Eli Lilly)
- Moderna vaccine → clinical correlates of protection

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates

K.S. Corbett, B. Flynn, K.E. Foulds, J.R. Francica, S. Boyoglu-Barnum, A.P. Werner, B. Flach, S. O'Connell, K.W. Bock, M. Minai, B.M. Nagata, H. Andersen,

HUMAN CONVALESCENT-PHASE SERUM

A panel of 42 human convalescent-phase serum specimens were obtained from persons between 18 and 84 years of age who had mild, moderate, or severe Covid-19 under institutional review board–approved specimen-collection protocols at the NIH Clinical Center (Bethesda, MD) (ClinicalTrials.gov number, NCT00067054), Aaron Diamond AIDS Research Center, Columbia University (New York) (NCT04342195), and the University of Washington (Seattle) (Hospitalized or Ambulatory Adults with Respiratory Viral Infection [HAARVI] study and STUDY00000959). Written informed consent was provided by all participants. Participants had a history of laboratory-confirmed SARS-CoV-2 infection roughly 1 to 2 months before they provided specimens.

Systems Serology to Evaluate Early Signatures Associated with COVID-19

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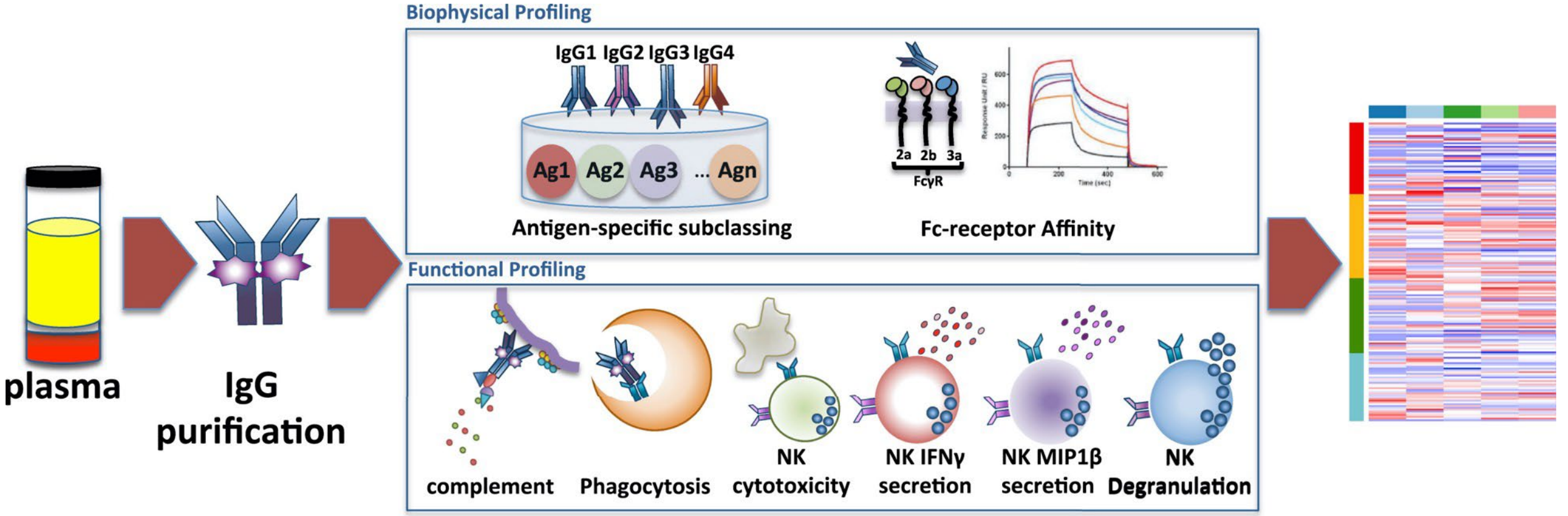
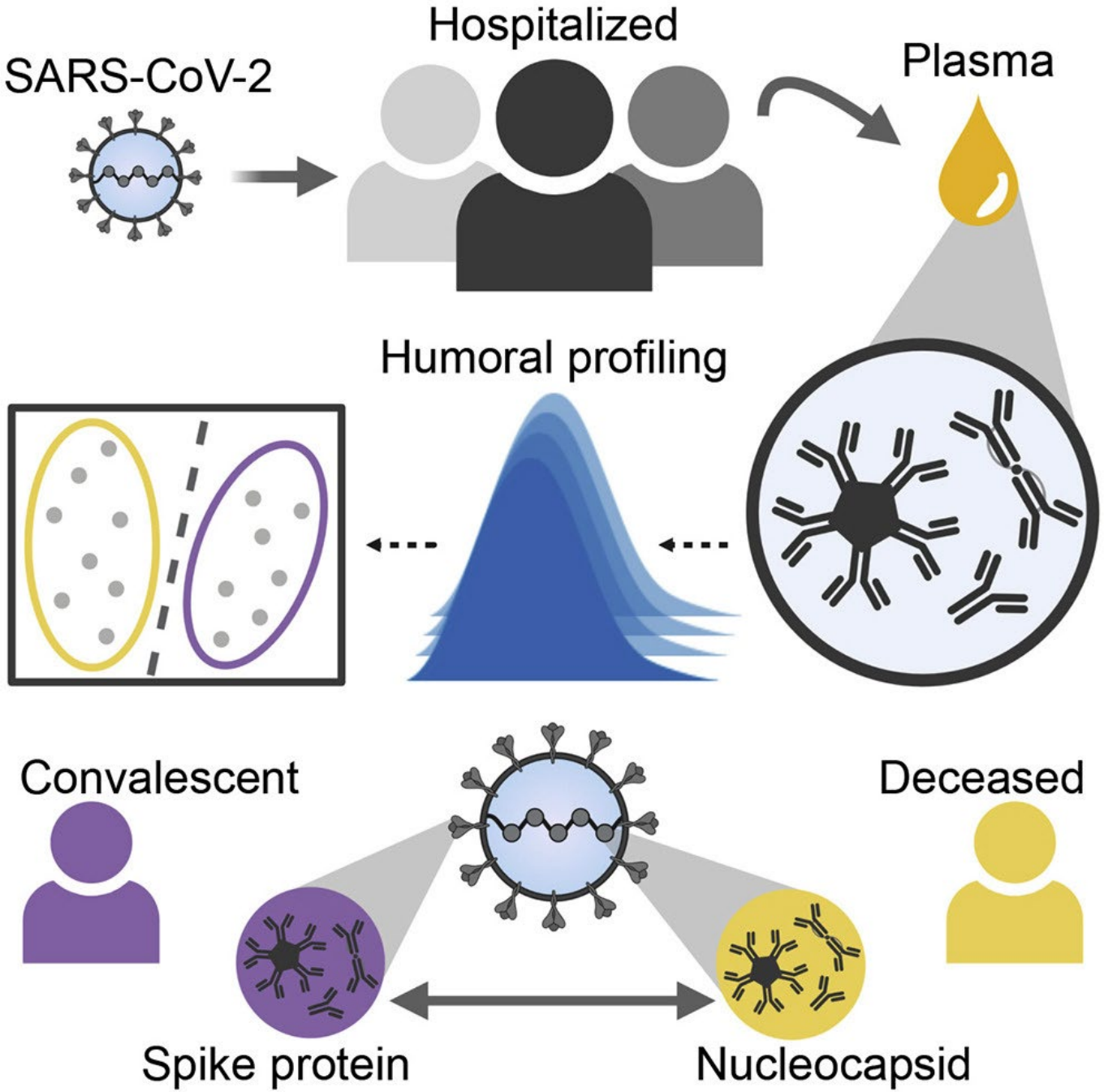
Hospitalized or Ambulatory Adults with Respiratory Viral Infections



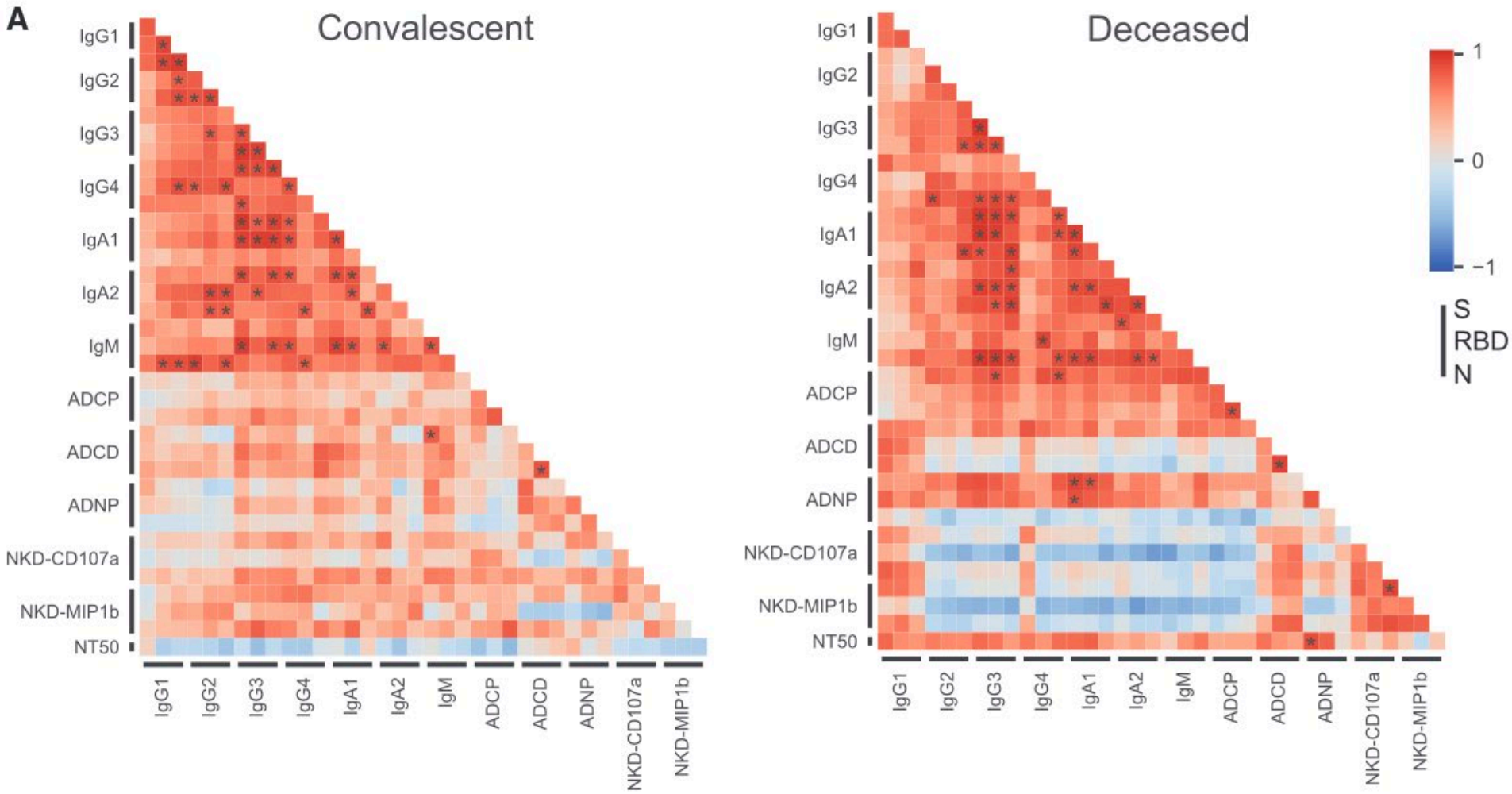
Atyeo, Immunity, 2020



Spike specific responses enriched in convalescent individuals, nucleocapsid responses in deceased individuals

Atyeo, Immunity, 2020

Heatmap showing pairwise correlation matrices of antigen-specific antibody titers and effector functions for convalescent vs deceased



Deceased individuals have negative and poorer correlations of NK cell-activating and complement-recruiting antibody responses with other functions

Atyeo, Immunity, 2020

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Hospitalized or Ambulatory Adults with Respiratory Viral Infections

Study Aims

- Characterize the prevalence of ongoing symptoms in a cohort of COVID-19 recovered individuals
- Describe changes in quality of life and ability to perform activities of daily living
- Compare these findings with a concurrent cohort of healthy controls

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Hospitalized or Ambulatory Adults with Respiratory Viral Infections

Long Term Sequelae of COVID: Methods

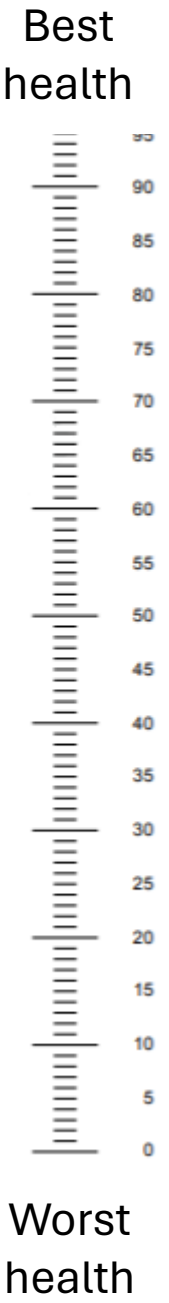
Initial questionnaire

- Completed at time of enrollment (either in the hospital at time of illness, or at day 30 after symptom onset at their first clinic visit)
- Assess acute symptoms

Follow up questionnaire completed 3-9 months after illness

- Persistent symptoms
- Activities of Daily Living
  - Climbing stairs, transferring, grooming & personal care, toilet & bathing
  - Household chores, managing personal affairs
- Medical care accessed
  - Primary care, Urgent Care, ED, hospitalization

Quality of life - EuroQol visual analog scale (based on the Italian COVID study)



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Hospitalized or Ambulatory Adults with Respiratory Viral Infections

Long Term Sequelae of COVID: Results

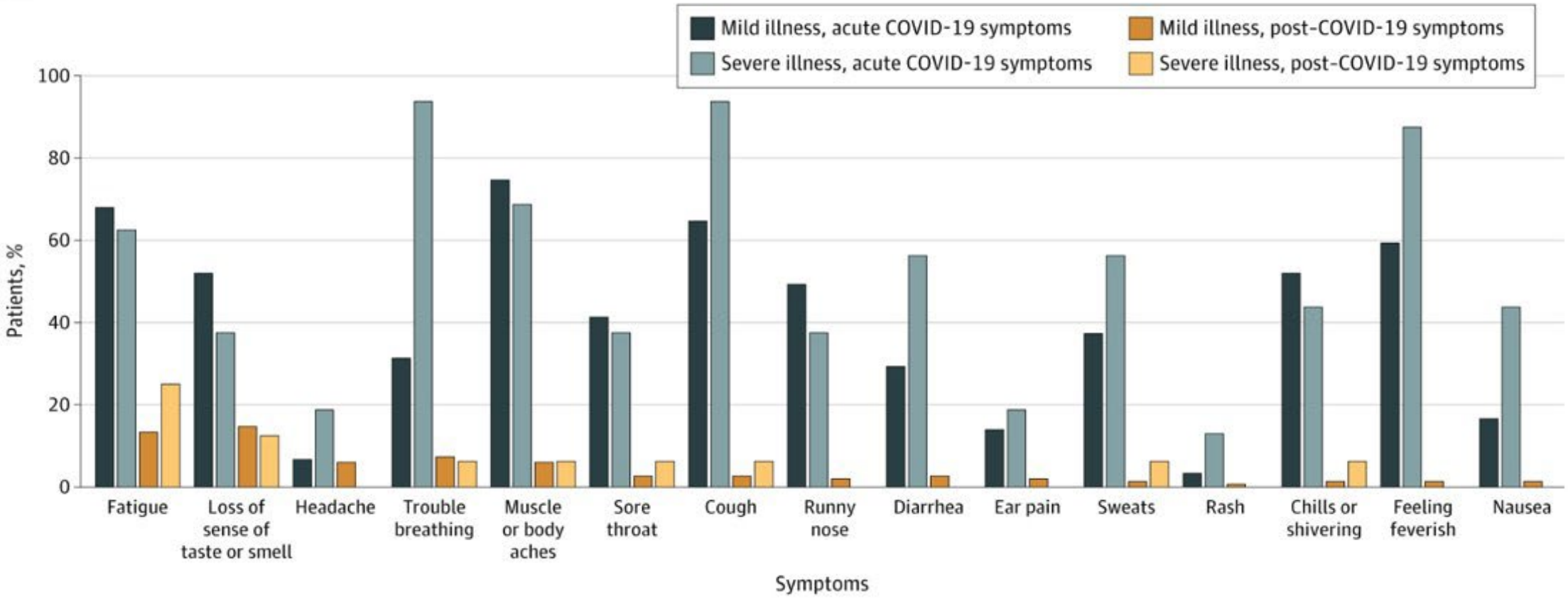
- 177 COVID-19 recovered individuals responded of 234 contacted (76%)
  - 161 mild-moderate cases (150 outpatients, 11 asymptomatic); 16 severe cases (16 inpatients)
- 21 healthy controls

- Completed survey median 5.5 months after illness
- At least one persistent symptom reported by:
  - 33% (n=49) of mild-moderate cases
  - 31% (n=5) of severe cases
- Persistent symptoms increased with age:
  - 27% (n=17) of 18-39 year olds
  - 30% (n=25) of 40-64 year olds
  - 43% (n=35) of those aged 65 and older

Logue JK, Franko NM, McCulloch DJ, ... Chu HY. 2021. Sequelae in Adults at 6 Months After COVID-19 Infection. JAMA Network Open

One-third of patients with mild disease had persistent symptoms at 6-month follow-up

B Percentage of participants who reported COVID-19 symptoms during acute illness and at follow-up



Logue JK et al, JAMA Network Open (2021); DOI: 10.1001/jamanetworkopen.2021.0830

CNN health Food Fitness Wellness Parenting Vital Signs • LIVE TV Edition

Almost a third of people with 'mild' Covid-19 still battle symptoms months later, study finds

By Dr. Sanjay Gupta, CNN Chief Medical Correspondent

Updated 9:28 AM ET, Tue February 23, 2021

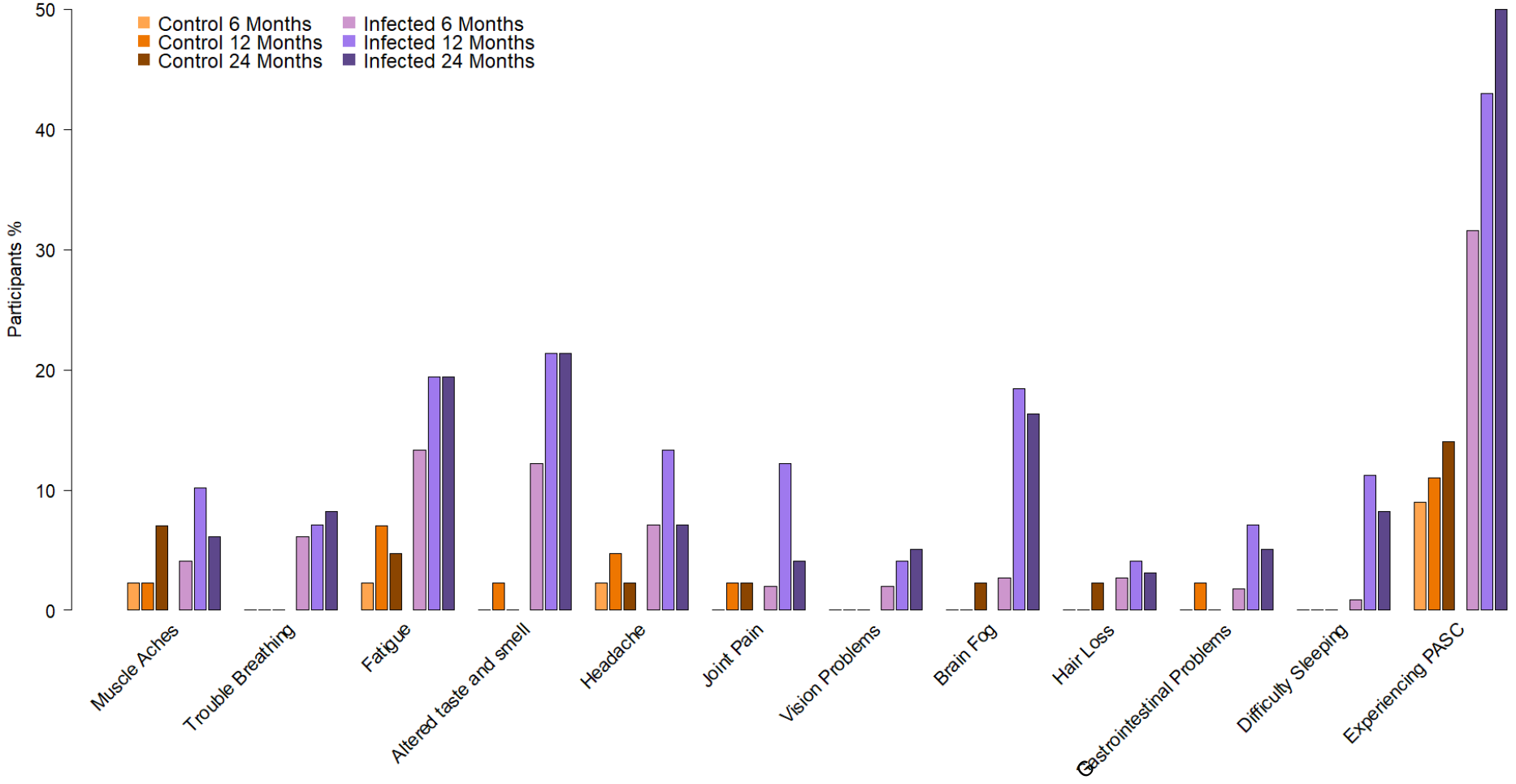
CNBC • WATCH LIVE

HEALTH AND SCIENCE

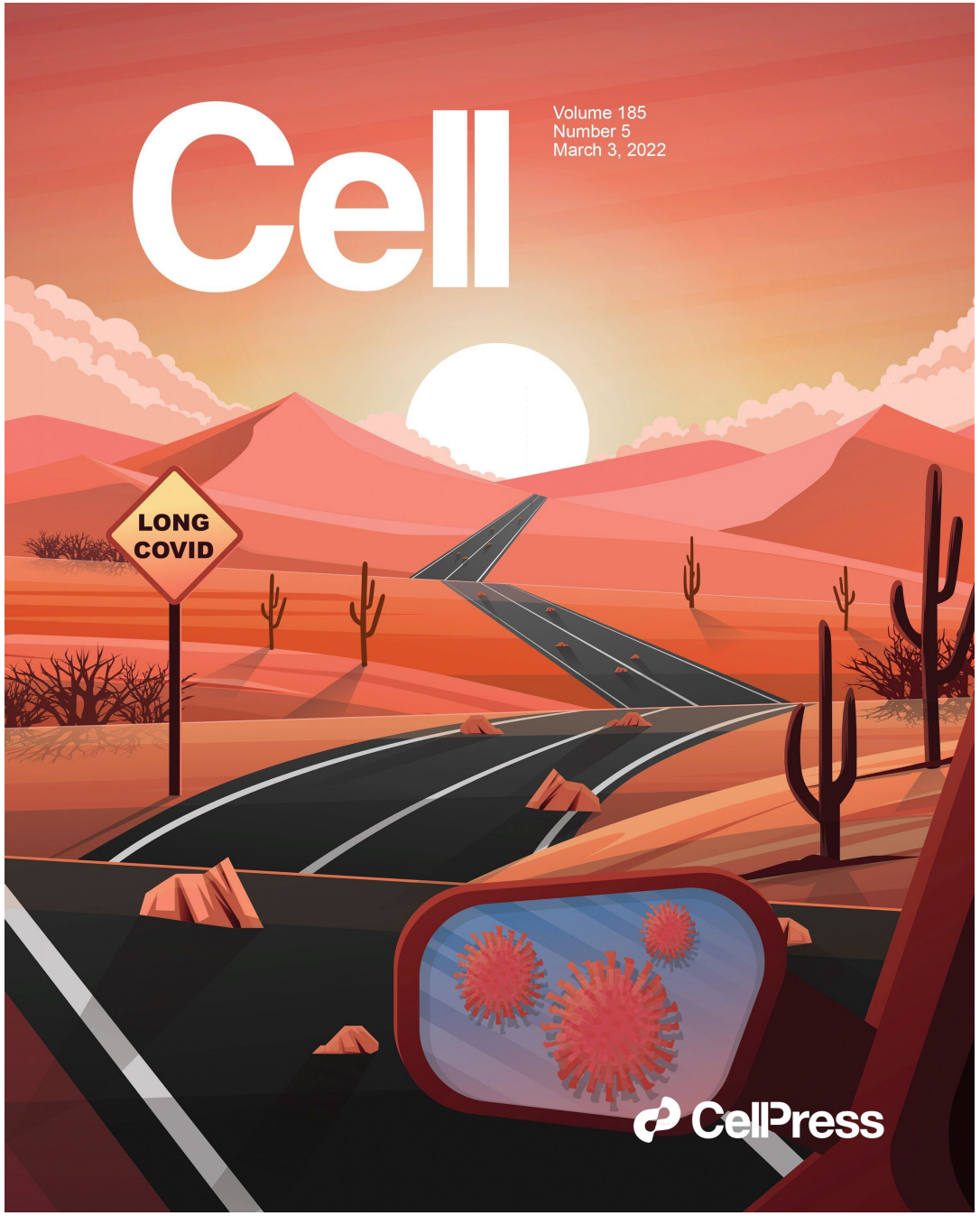
Dr. Fauci says new data suggests 'long' Covid symptoms can last up to 9 months

PUBLISHED WED, FEB 24 2021•12:03 PM EST UPDATED WED, FEB 24 2021•1:01 PM EST

Long COVID Persists 24 Months after Infection



- 50% (56/112) of participants experienced symptoms of long COVID at 24 months
- Most common symptoms
  - Altered smell and taste
  - Fatigue
  - Brain fog
- 36% reported conditions were improving or resolved



The New York Times

The Coronavirus Pandemic › | Covid-19 Updates | Coronavirus Map an

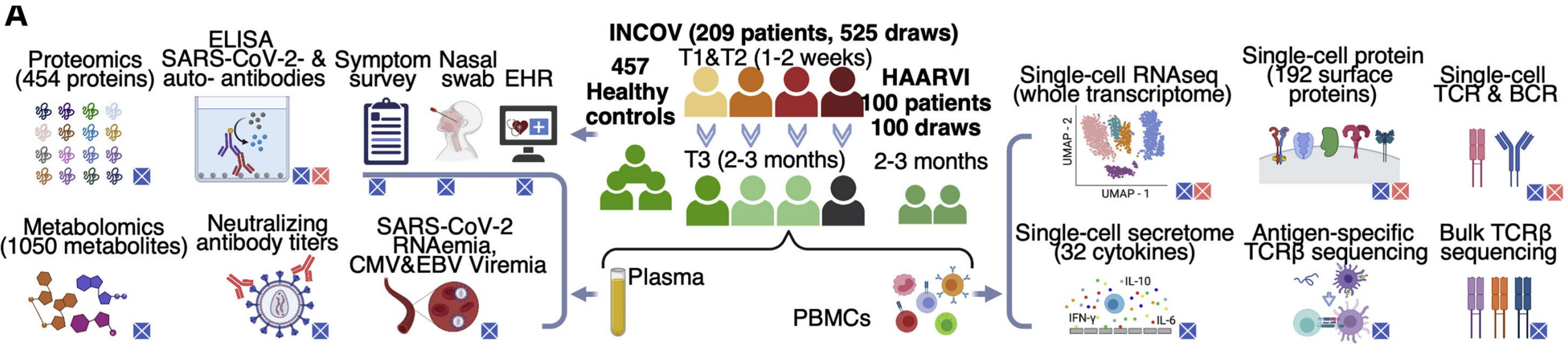
New Research Hints at 4 Factors That May Increase Chances of Long Covid

If further study confirms the findings, they could lead to ways to prevent and treat the complex condition.

Give this article

Su, Cell, 2022

Overview of study design: two COVID-19 cohorts and uninfected controls



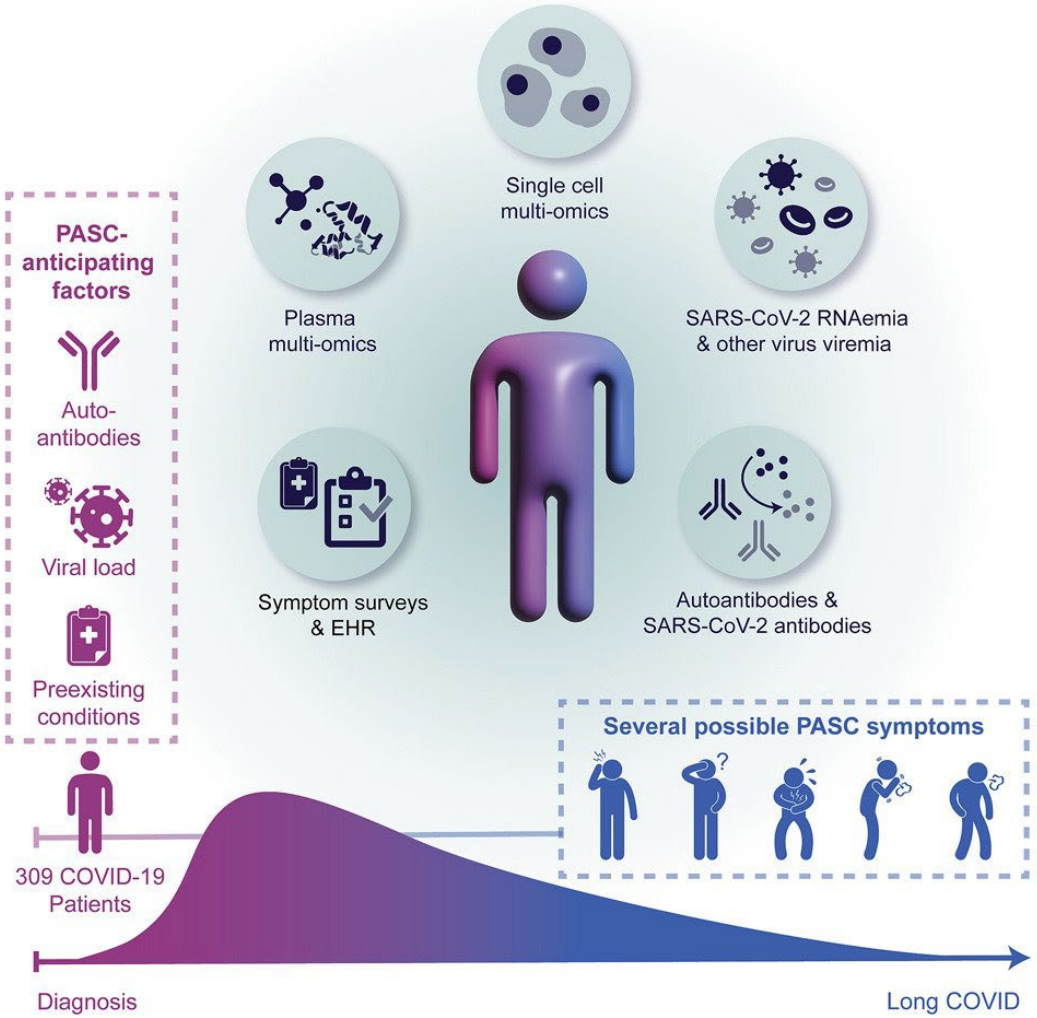
- Clinical and laboratory data
- Autoantibodies
- Plasma proteomic and metabolomic profiling

Three time points
T1: Acute illness
T2: 1-2 weeks
T3: 2-3 months

- Single cell multi-omic characterization

Su, Cell, 2022

Early Factors Correlated with Long COVID

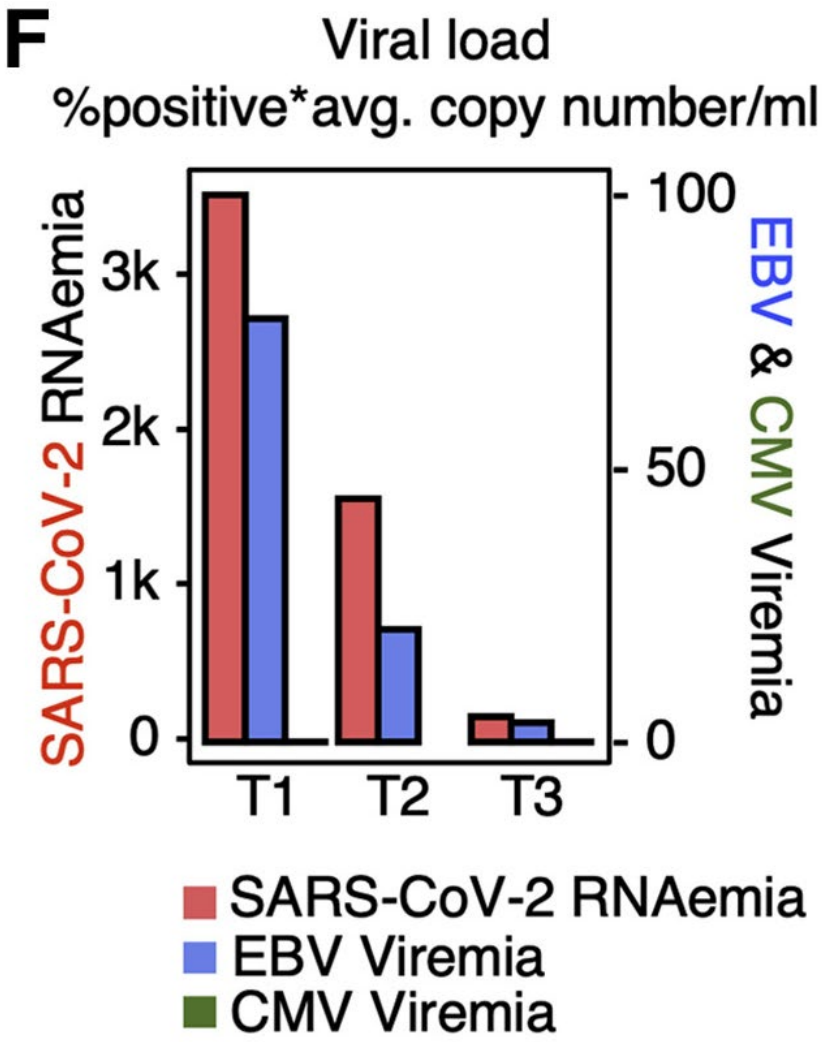


4 PASC-anticipating risk factors at time of initial COVID-19 diagnosis:

- Epstein-Barr virus viremia
- SARS-CoV-2 RNAemia
- Type 2 diabetes
- Autoantibodies

Su, et al., Cell (2022) DOI: 10.1016/j.cell.2022.01.014

EBV and SARS-CoV-2 viremia at initial diagnosis was common, and associated with long COVID

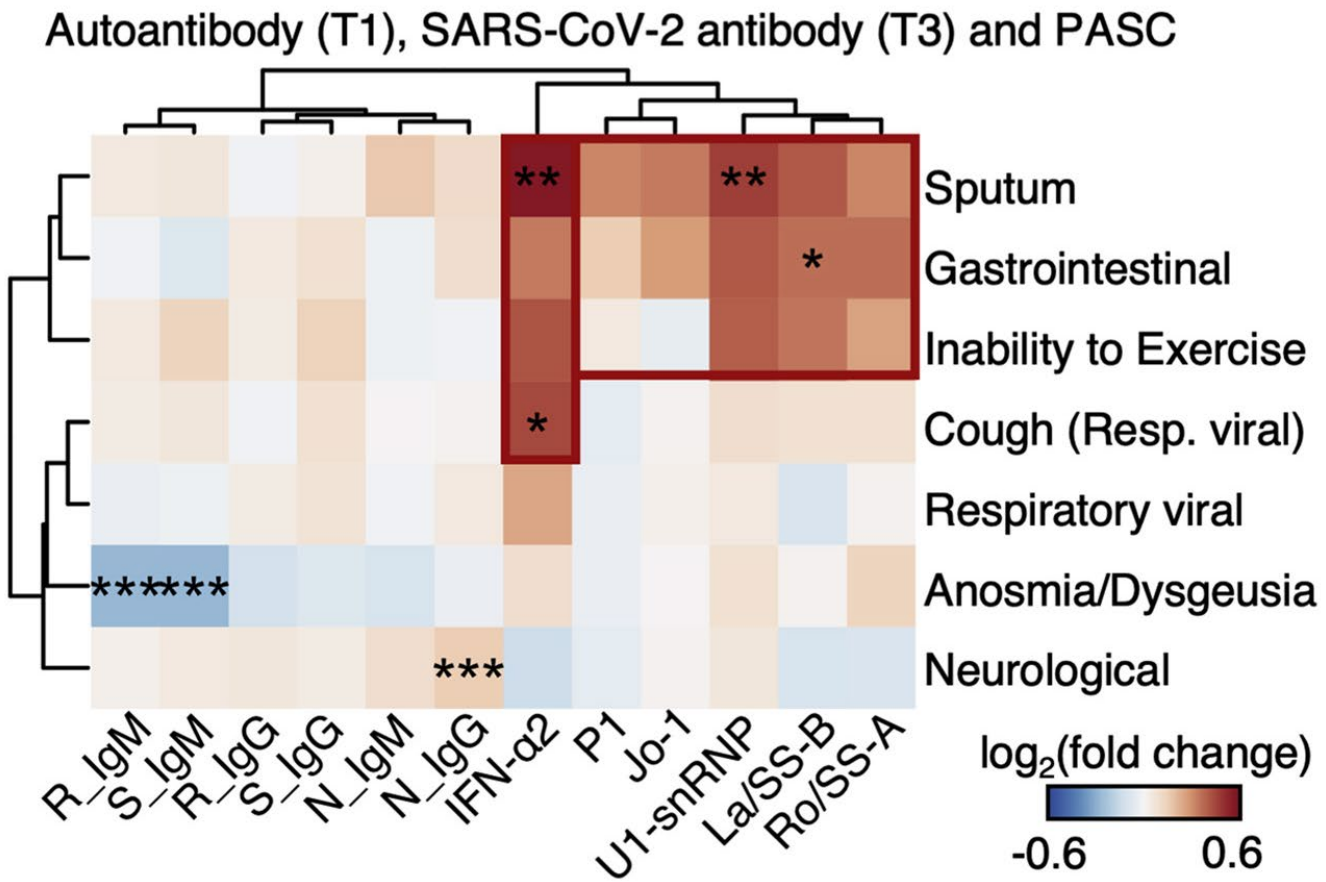


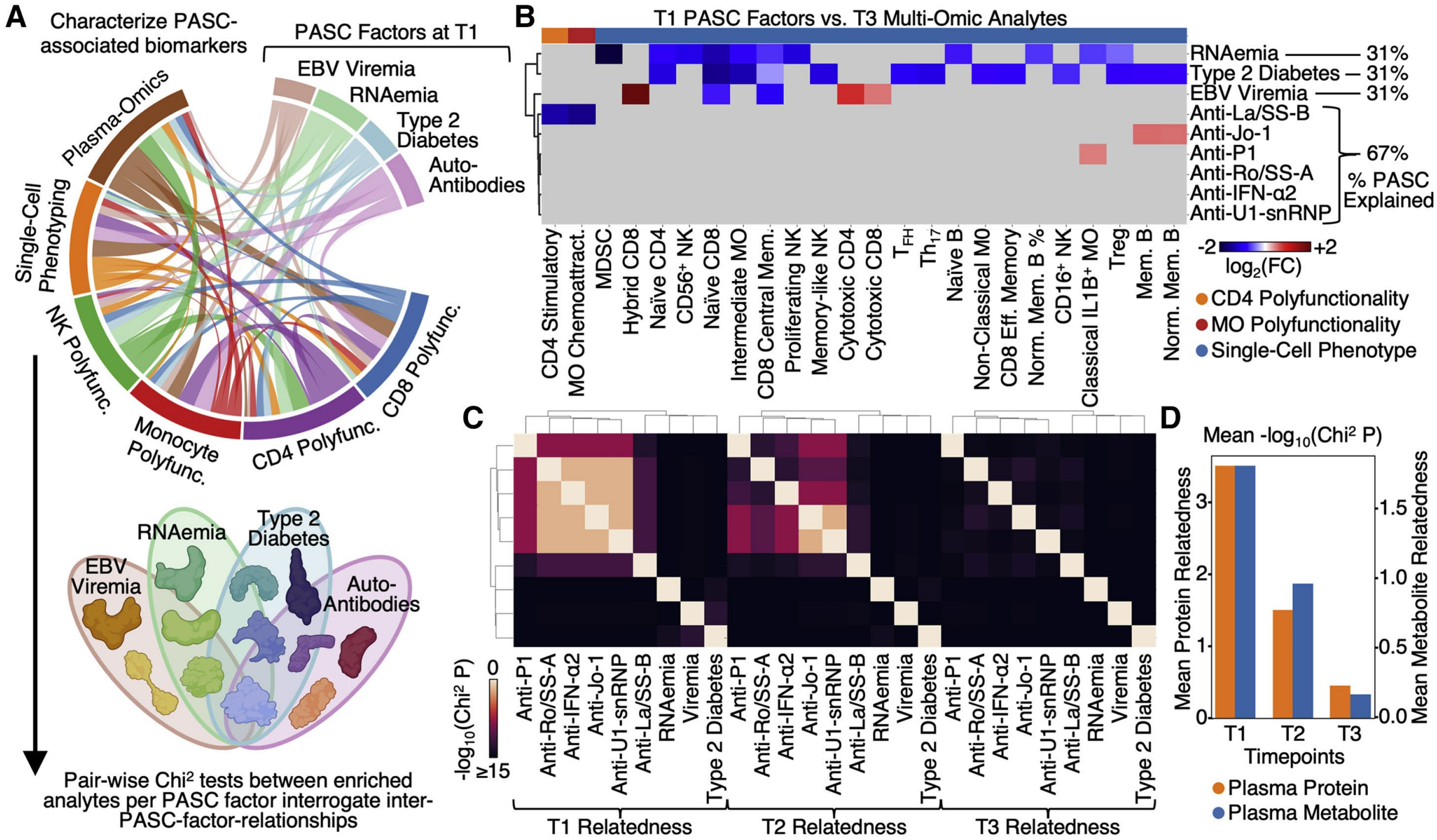
High proportions of individuals with SARS-CoV-2 and EBV at acute diagnosis

- 14% with EBV viremia
- 25% with SARs-CoV-2 RNAemia
- Resolved by 2-3 months

Autoantibodies present early in illness, and associated with specific long COVID conditions at 2-3 months

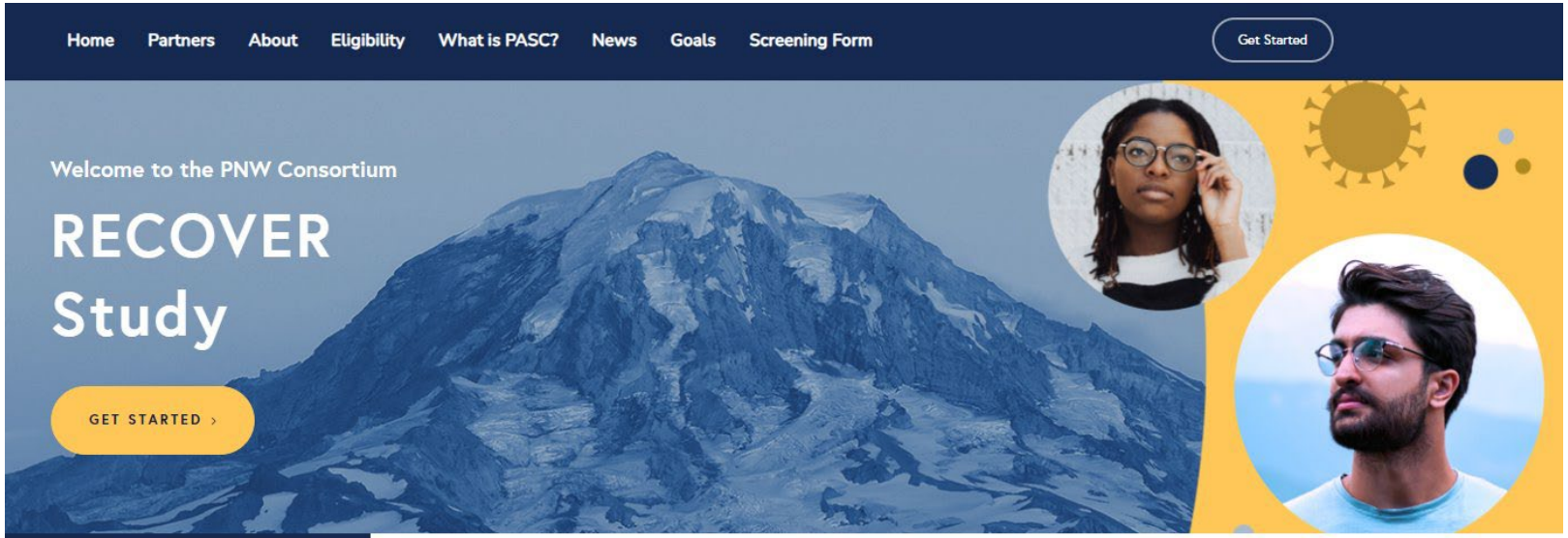
- Investigated autoantibodies commonly associated with systemic lupus erythematosus
- GI, inability to exercise and sputum production associated with autoantibodies
- Many with autoantibodies at 2-3 months had mature autoantibodies at early time points (i.e. could autoimmune disease predate long COVID)
- Higher SARS-CoV-2 antibody was associated with lower autoantibodies
- SARS-CoV-2 nucleocapsid IgG associated with neurologic symptoms

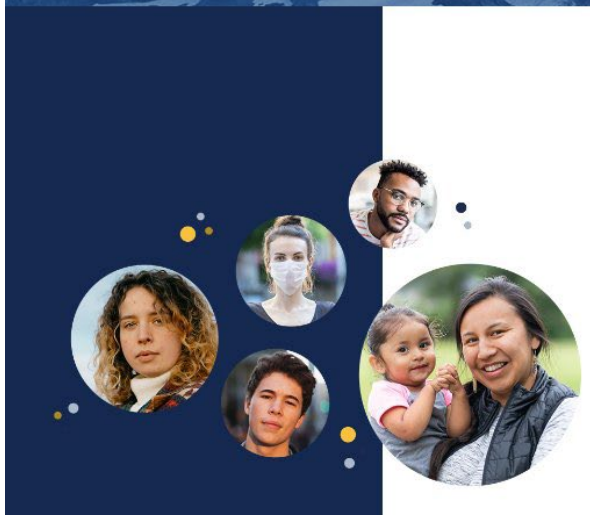



A
Characterize PASC-associated biomarkers
PASC Factors at T1
EBV Viremia
RNAemia
Type 2 Diabetes
Auto-Antibodies
Plasma-Omics
Single-Cell Phenotyping
NK Polyfunc.
Monocyte Polyfunc.
CD4 Polyfunc.
CD8 Polyfunc.
Pair-wise Chi² tests between enriched analytes per PASC factor interrogate inter-PASC-factor-relationships
B
T1 PASC Factors vs. T3 Multi-Omic Analytes
RNAemia — 31%
Type 2 Diabetes — 31%
EBV Viremia — 31%
Anti-La/SS-B
Anti-Jo-1
Anti-P1
Anti-Ro/SS-A
Anti-IFN-α2
Anti-U1-snRNP
67%
% PASC Explained
CD4 Stimulatory
MO Chemoattract.
MDSC
Hybrid CD8
Naïve CD4
CD56⁺ NK
Naïve CD8
Intermediate MO
CD8 Central Mem.
Proliferating NK
Memory-like NK
Cytotoxic CD4
Cytotoxic CD8
T_FH
Th_17
Naïve B
Non-Classical M0
CD8 Eff. Memory
Norm. Mem. B %
CD16⁺ NK
Classical IL1B⁺ MO
Treg
Mem. B
Norm. Mem. B
-2
+2
log₂(FC)
CD4 Polyfunctionality
MO Polyfunctionality
Single-Cell Phenotype
C
-log₁₀(Chi² P)
0
≥15
Anti-P1
Anti-Ro/SS-A
Anti-IFN-α2
Anti-Jo-1
Anti-U1-snRNP
Anti-La/SS-B
RNAemia
Viremia
Type 2 Diabetes
T1 Relatedness
T2 Relatedness
T3 Relatedness
D
Mean -log₁₀(Chi² P)
Mean Protein Relatedness
Mean Metabolite Relatedness
T1
T2
T3
Timepoints
Plasma Protein
Plasma Metabolite

NIH RECOVER Observational Study

NIH consortium with 40,000 participants nationwide





Help us better understand the long-term effects of COVID.

If you or someone in your family has had COVID, or are feeling the long term effects of COVID, you might be able to help us understand more about it and treat it. Even if you have not had COVID, you might be able to help.

GET STARTED ›

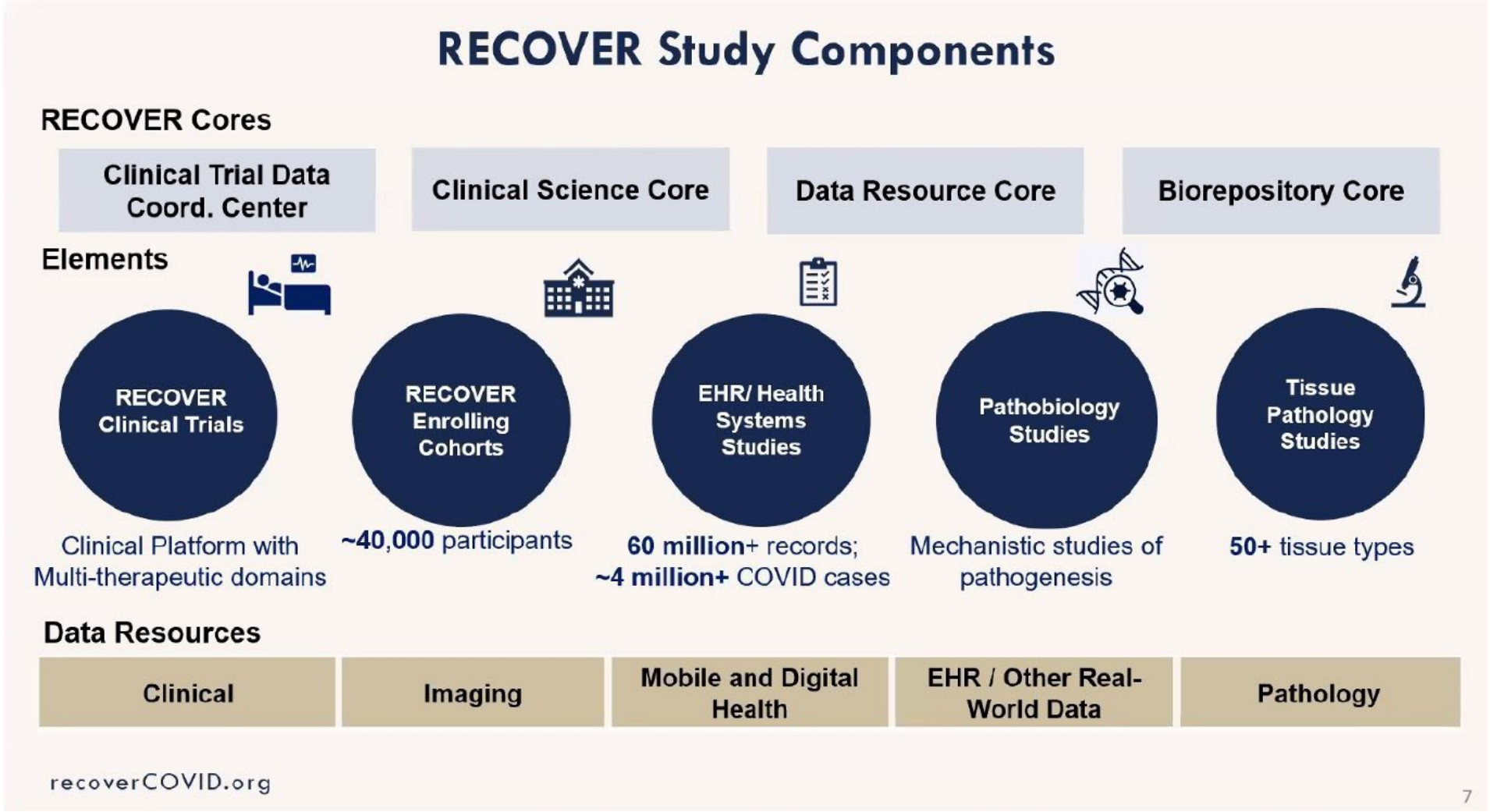
RECOVER
Researching COVID to Enhance Recovery

ISB
UNIVERSITY of WASHINGTON
SWEDISH
Cedars Sinai
Providence

Study Aims

- Characterize the incidence and prevalence of sequelae of SARS-CoV-2 infection
  - Acute infected cohort (<30 days since infection)
  - Post-acute infected cohort (>30 days since infection)
  - Uninfected controls
- Characterize and describe the spectrum of clinical symptoms
- Define the biological mechanisms underlying pathogenesis of the sequelae of SARS-CoV-2 infection

RECOVER Observational Study Components



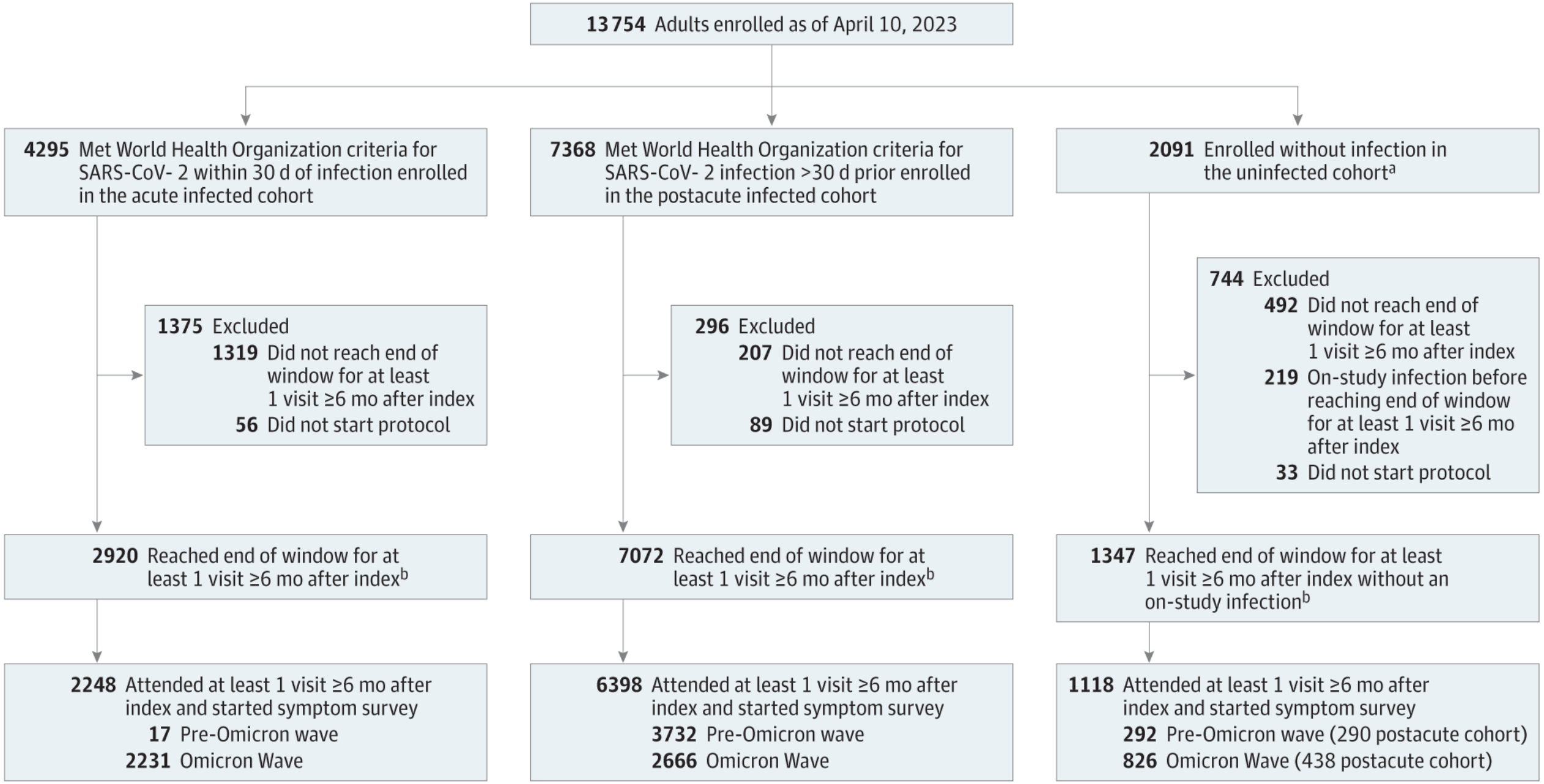
Timeline of Study Activities for Participants enrolled into the prospective observational study

		Time Point after index date															
eCRF	Baseline	3m	6m	9m	12m	15m	18m	21m	24m	27m	30m	33m	36m	39m	42m	45m	48m
Enrollment	●																
Tier 1-2 Consent	●																
Identity	●																
Visit	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Comorbidities	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
COVID Treatment*	●																
Medications	●																
Change in Medications		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Demographics	●																
PASC Symptoms	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Vaccination Status	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Social Determinants of Health	●																
Social Determinants Follow-up		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Alcohol/Tobacco	●																
Alcohol/Tobacco Follow-up		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Disability	●																
Pregnancy	●																
Pregnancy Follow-up		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Tier 1 office visit	●		●		●				●				●				●
Biospecimens	●	●	●		●				●				●				●
Lab Results	●	●	●		●				●				●				●
Tier 2/Tier 3 Tests																	

* COVID Treatment not collected on people without infection

Legend

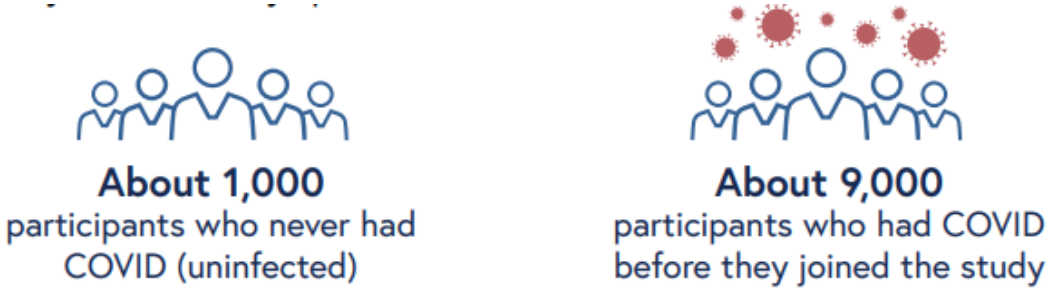
- ● Completed by research coordinator
- ● Completed by participant
- ● Completed by research coordinator with review/validation by participant

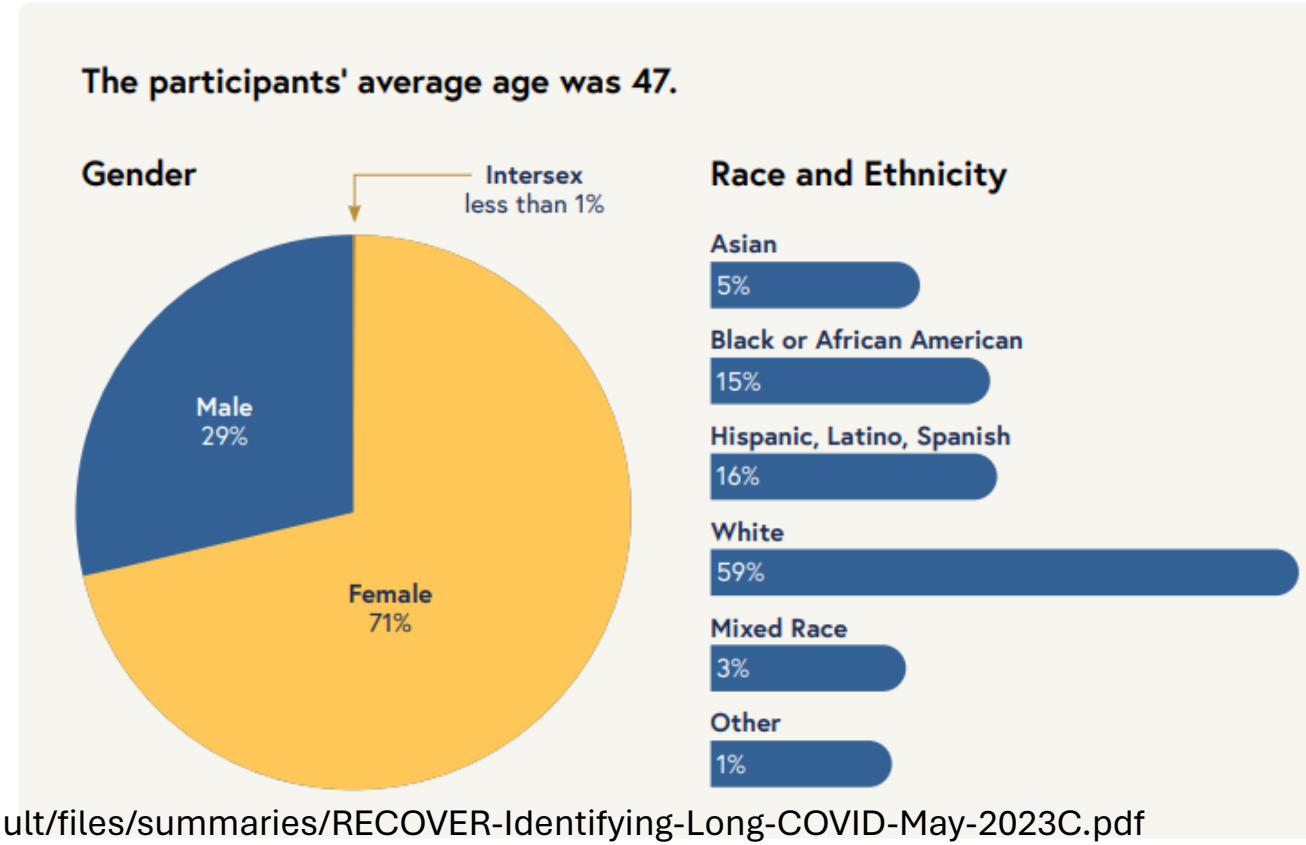


T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

RECOVER: Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

- What are the defining symptoms of Long COVID?
- Compared symptoms reported in individuals who never had COVID against those who had COVID at least six months prior
- Evaluated 9764 individuals (89% SARS-CoV-2 infection) enrolled before April 2023 with at least six months of follow-up



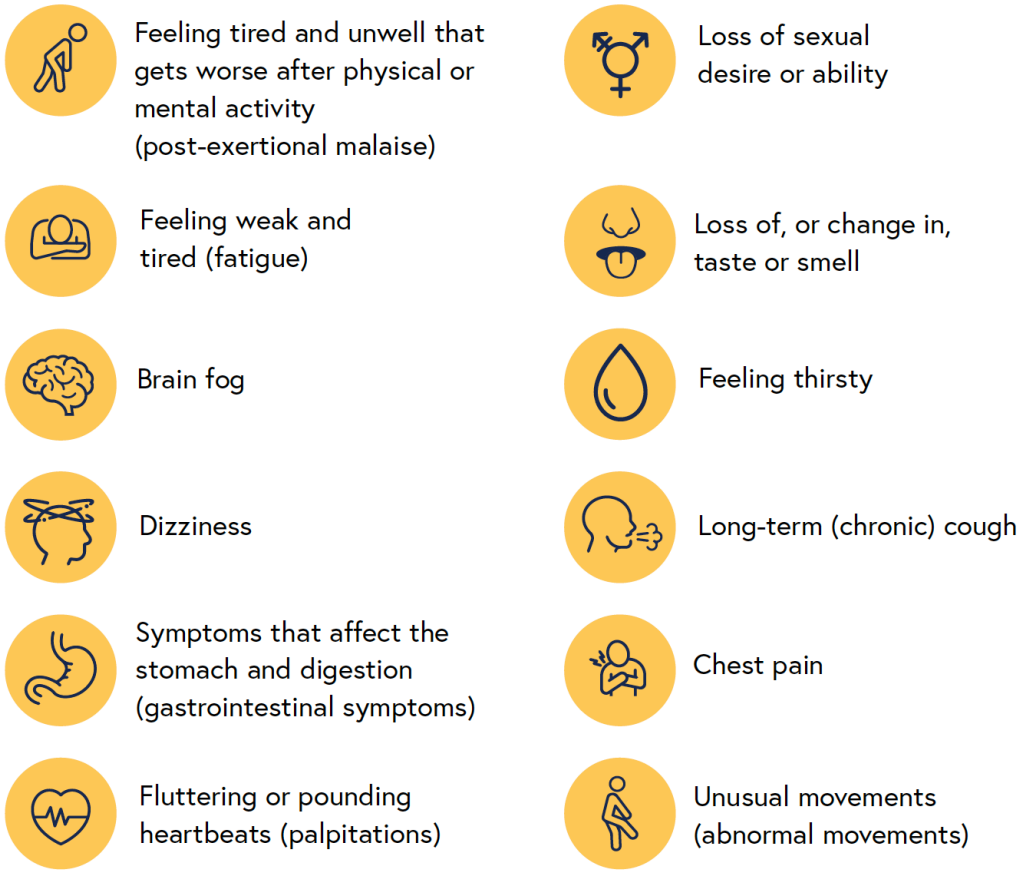


T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

RECOVER: Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

- 10% of previously infected participants developed long COVID
- Evaluated 37 symptoms: selected 12 symptoms with adjusted odds ratio 1.5 or greater in those who had COVID, compared to uninfected
- Individuals were more likely to have long COVID
  - First COVID infection before December 2021 (Omicron wave)
  - Had more than one infection
  - Did not receive the COVID-19 vaccine

- Overall 12 symptoms best identified those with long COVID



T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

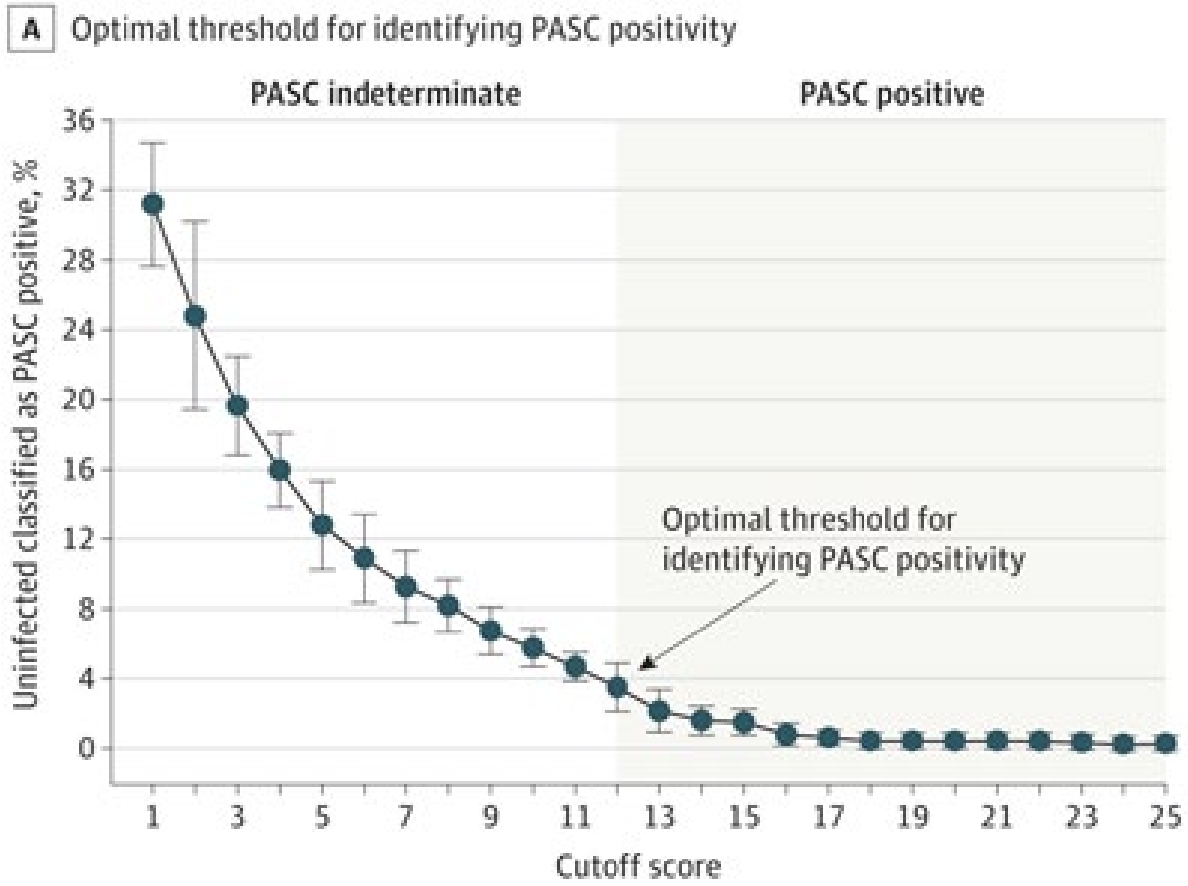
RECOVER: Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

- LASSO used to identify which symptoms defined PASC
- Symptom score assigned by dividing estimated log odds ratio by 0.10
- For each person, total score is sum of scores for each symptom reported
- Score threshold of 12 was optimal for separating those with and without PASC

Table 2. Model-Selected Symptoms That Define PASC and Their Corresponding Scores[a]

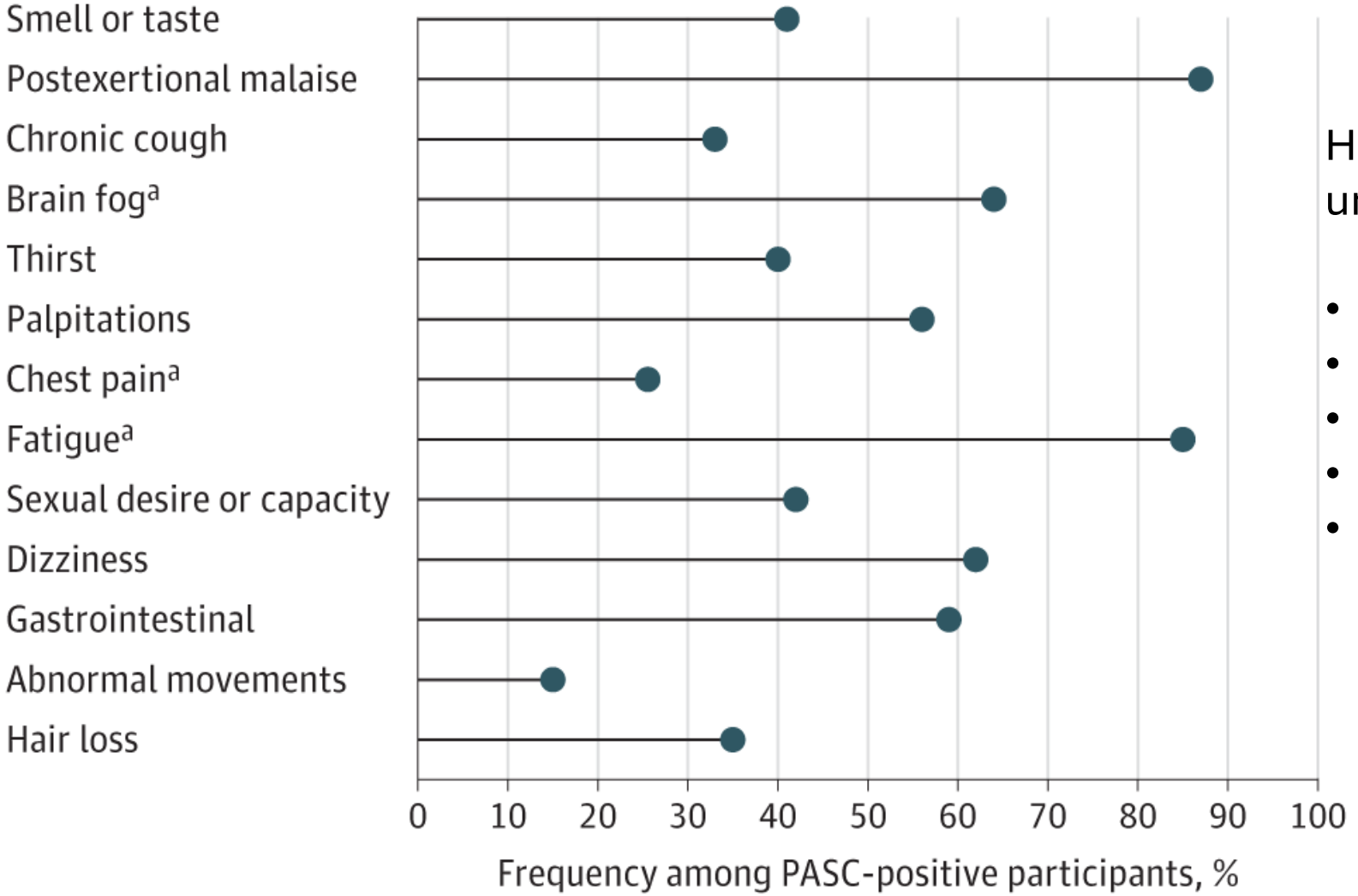
Symptom	Log odds ratio	Score
Smell/taste	0.776	8
Postexertional malaise	0.674	7
Chronic cough	0.438	4
Brain fog[b]	0.325	3
Thirst	0.255	3
Palpitations	0.238	2
Chest pain[b]	0.233	2
Fatigue[b]	0.148	1
Sexual desire or capacity	0.126	1
Dizzines	0.121	1
Gastrointestinal	0.085	1
Abnormal movements	0.072	1
Hair loss	0.049	0

RECOVER: Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection



T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

RECOVER: Symptom frequencies among PASC-positive participants for symptoms that contribute to the PASC score.



Highest OR for infected vs. uninfected:

- Postexertional malaise (aOR 5.2)
- Fatigue (aOR 2.9)
- Dizziness (aOR 3.4)
- Brain fog (aOR 4.5)
- GI symptoms (aOR 2.7)

T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

RECOVER: Patient-Reported Outcomes of quality of life, physical health and ability to carry out physical activities decreases as PASC score increases

C Distribution of PROMIS Global 10 responses

PROMIS Global 10 Q2: general quality of life

	0	1-2	3-6	7-11	12-16	≥17
Excellent	29	17	13	12	6	4
Very good	44	46	38	36	22	17
Good	21	30	37	36	41	32
Fair	5	6	10	14	25	33
Poor	1	0	2	2	7	14
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

PROMIS Global 10 Q3: general physical health

	0	1-2	3-6	7-11	12-16	≥17
Excellent	15	6	4	4	1	0
Very good	41	31	27	20	11	7
Good	31	43	42	41	34	26
Fair	10	18	24	29	42	41
Poor	1	1	4	6	12	26
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

PROMIS Global 10 Q6: ability to carry out everyday physical activities

	0	1-2	3-6	7-11	12-16	≥17
Completely	78	71	59	47	27	15
Mostly	12	17	21	25	27	22
Moderately	6	9	14	20	28	30
A little	3	3	6	8	17	31
Not at all	0	0	0	0	1	1
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

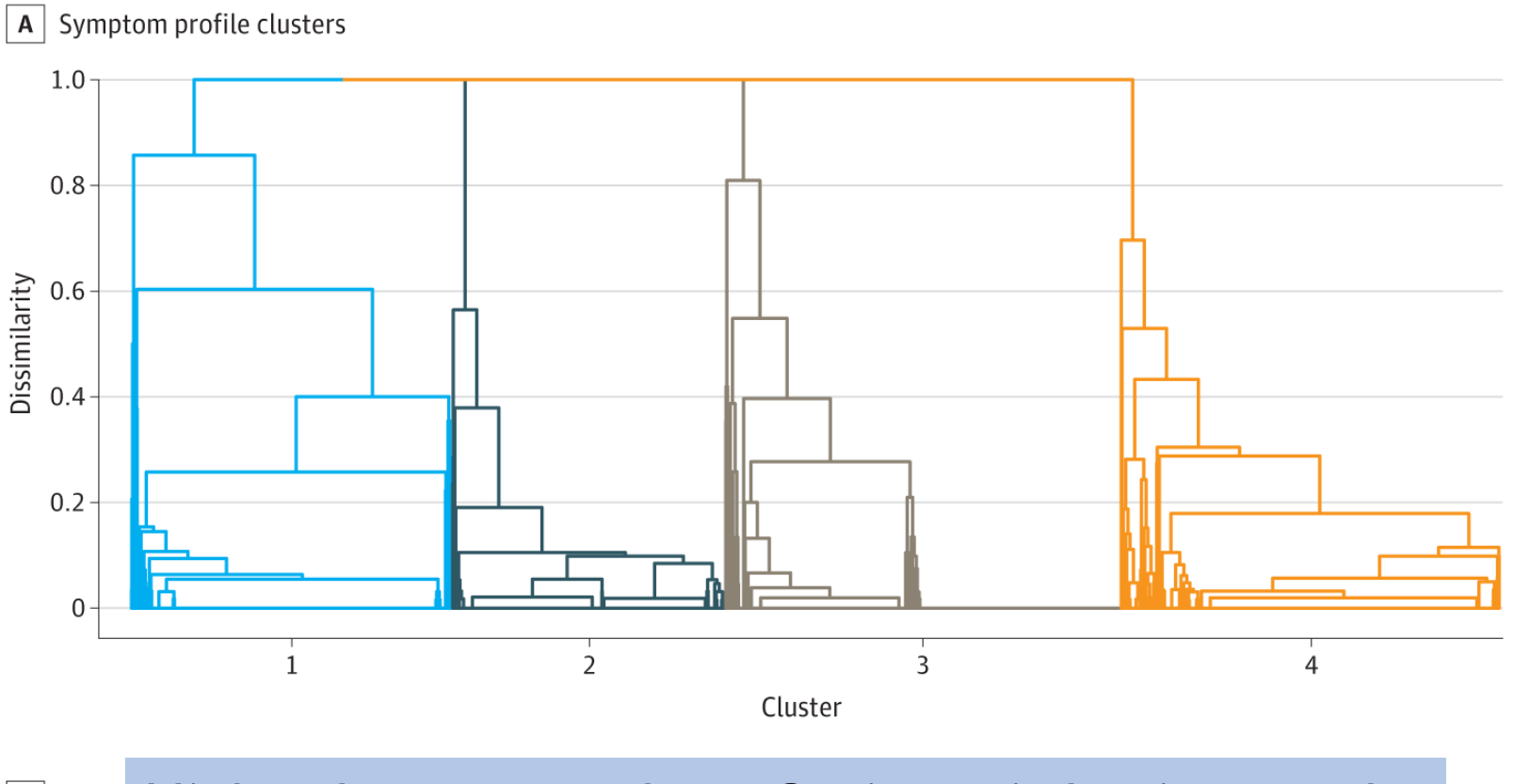
Identification of Postacute Sequelae of SARS-CoV-2 Infection (PASC) Subgroups and Their Characteristics

Cluster 1: Smell or taste

Cluster 2: Postexertional malaise, fatigue

Cluster 3: brain fog, postexertional malaise, fatigue

Cluster 4: fatigue, postexertional malaise, dizziness, brain fog, palpitations



Higher frequency of pre-Omicron infections and unvaccinated participants in Cluster 4 (most severe)

T. Thaweethai, et al. JAMA. May 2023 & https://recovercovid.org/sites/default/files/summaries/RECOVER-Identifying-Long-COVID-May-2023C.pdf

Outline

- Definitions, risk factors, and clinical manifestations
- Results from research studies at the University of Washington
- New clinical trials

RECOVER-NEURO Clinical Trial

RECOVER-NEURO is focused on cognitive dysfunction symptoms associated with Long COVID, which may include trouble thinking clearly or remembering things (brain fog) and problems focusing on tasks. We want to better understand how the virus that causes COVID-19 affects the brain and find possible treatments to improve brain function for people with Long COVID.

RECOVER

Researching COVID to Enhance Recovery

RECOVER NEURO

Participants will be assigned by chance to one of these groups:

BrainHQ	BrainHQ active comparator	BrainHQ + PASC-CoRE	BrainHQ + tDCS-active	BrainHQ + tDCS-comparator

Participants will be in RECOVER-NEURO for about 6 months, including a 10-week study intervention period. During this time, they will be asked to:

- Visit the clinic 3 times
- Complete brain training sessions at home for 10 weeks
- Answer surveys about how they are feeling
- Complete lab tests and brain function tests

RECOVER-VITAL Clinical Trial

RECOVER-VITAL (viral persistence and reactivation, and immune dysregulation) is focused on viral persistence, which is when the virus that causes COVID-19 stays in the body and causes damage to organs or the immune system (the body's system that fights off illnesses) to not function properly. Researchers think that viral persistence may lead to Long COVID symptoms.

RECOVER
Researching COVID to Enhance Recovery

RECOVER VITAL

Participants will be assigned by chance to one of these groups:

PAXLOVID (nirmatrelvir and ritonavir) 25 days	PAXLOVID 15 days + Ritonavir and placebo 10 days	Ritonavir and placebo 25 days

Participants will be in RECOVER-VITAL for about 6 months.
During this time, they will be asked to:

- Visit the clinic 4 to 5 times
- Answer surveys about how they are feeling
- Take a study drug for up to 25 days, provided at no cost
- Complete lab tests, physical ability tests, and/or brain function tests

Conclusions

- Long COVID is a multisystem condition that occurs in approximately 10% of individuals with COVID-19 infection
- Certain risk factors present at initial diagnosis, including EBV viremia, SARS-CoV-2 RNAemia, diabetes, and autoantibodies are associated with development of long COVID
- Certain distinct symptoms are associated with long COVID, including post-exertional malaise, brain fog, fatigue and GI symptoms
- New research studies are attempting to better understand the predictors of PASC, as well as potential preventions and treatments

Thank you to the HAARVI participants who have participated in our studies for the past four years

Team HAARVI: Jennifer Logue, Helen Nguyen, Kino Watanabe, Kristen Huden, Anna Elias-Warren, Ariana Magedson, Erica Clark, Tiffany Mei, Nicholas Franko, Dylan McDonald

haarvi

Hospitalized or Ambulatory Adults with Respiratory Viral Infections



Andy McGuire Leo Stamatatos Julie McElrath

Chetan Seshadri


Barney Graham NIH VRC Galit Alter Ragon Institute


Rob Carnahan, Jim Crowe Vanderbilt University

Julie Overbaugh

Jesse Bloom

Mike Gale

Jim Heath

Josh Schiffer

Jenny Lund

David Veesler

Steve Elledge
Dan Barouch
Deb Fuller
Neil King
Wes Van Voorhis

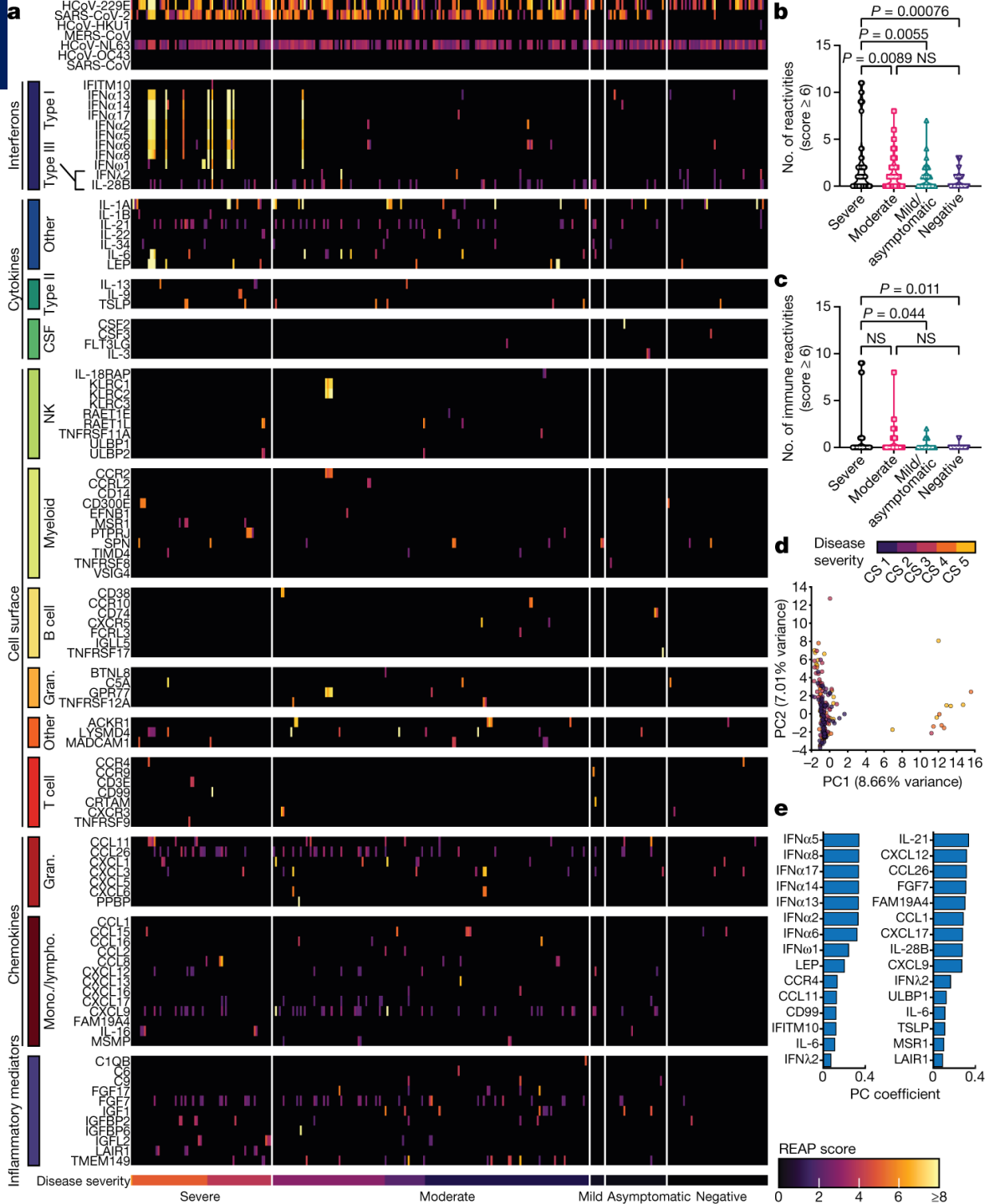
Research and clinical care

- https://www.chulab.org/participate-in-a-study
  - Enroll in observational and clinical trials
- https://www.uwmedicine.org/specialties/post-covid-rehabilitation
  - Access medical care at UW

Other mechanisms: Autoantibodies

Immune-targeting autoantibodies are increased in patients with COVID-19:

- Acute COVID-19 associated with increased autoantibody reactivities including auto-Ab against:
  a. Immunomodulatory proteins (cytokines, chemokines, complement components and cell-surface proteins)
  b. Tissue-associated antigens

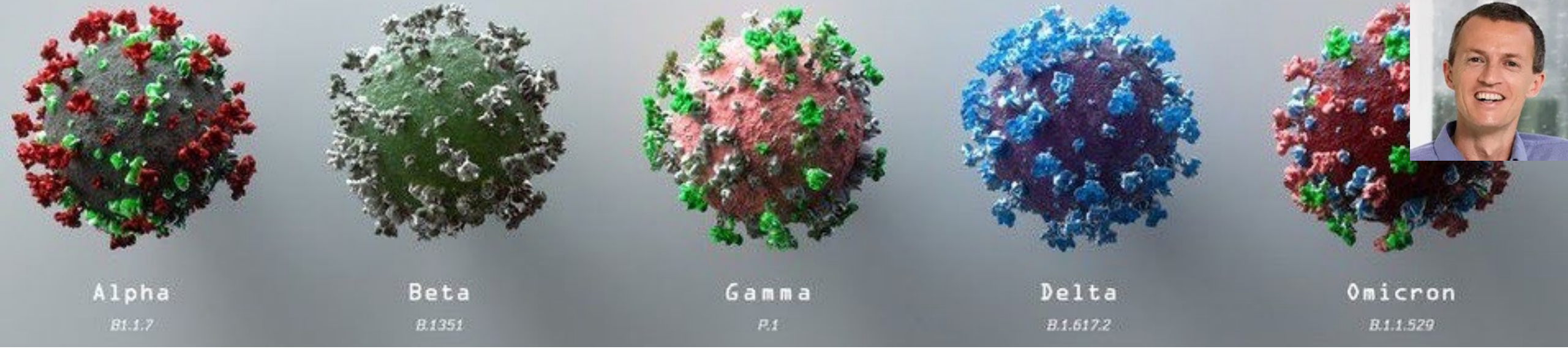


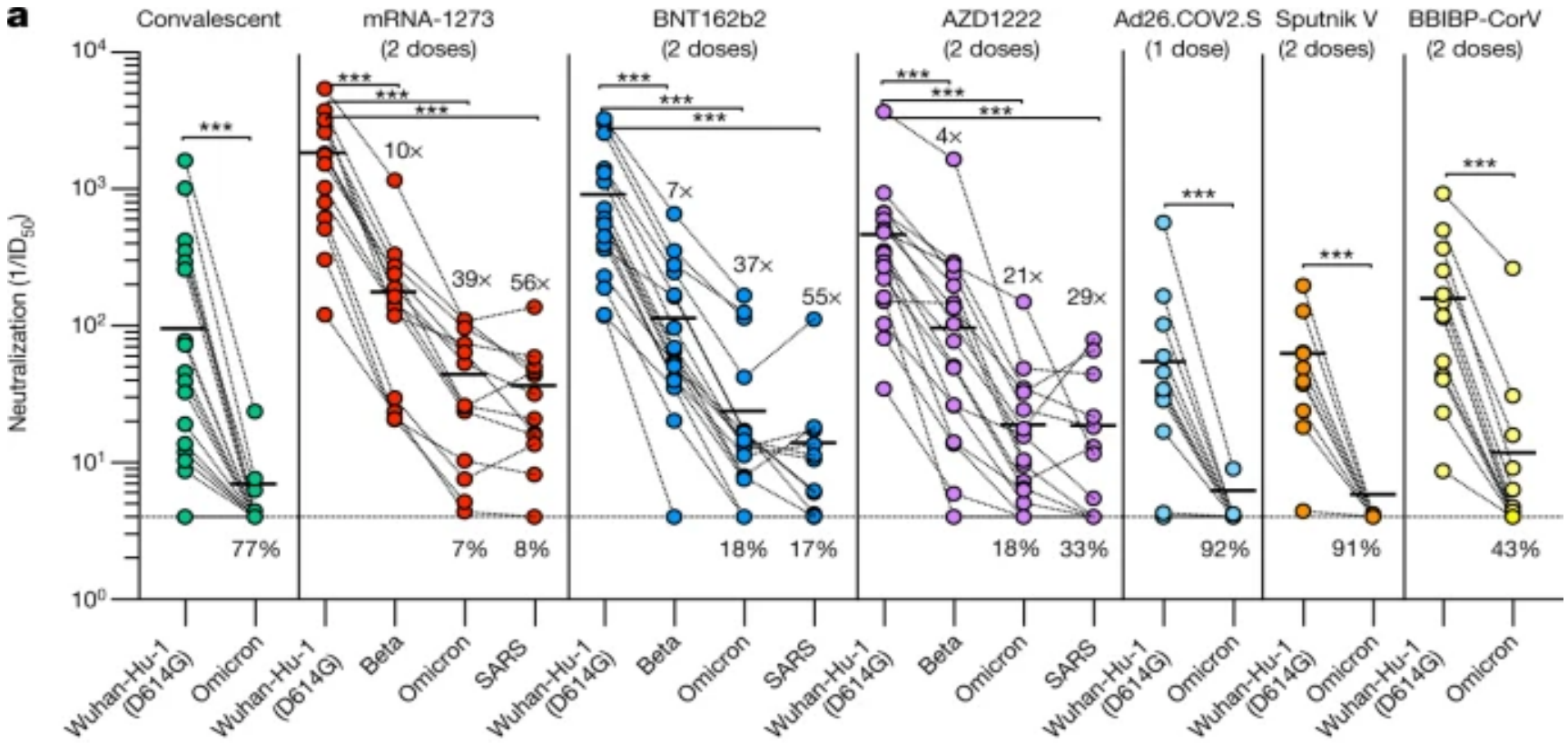
Wang EY, Nature (2021);
https://doi.org/10.1038/s41586-021-03631-y

Slide courtesy of Jason Goldman, MD, MPH

Table 1. RECOVER Adult Cohort Demographic Characteristics by Infection Status at Enrollment

Characteristic[a]	No./total (%)		
	Infected (n = 8646)	Uninfected (n = 1118)	Uninfected with balancing weights (n = 1109), %
Age at enrollment, y			
Median (IQR)	45 (34-59)	55 (40-65)	45 (35-60)
No.	8637	1117	1109
Age category at enrollment, y			
18-45	4389/8637 (51)	377/1117 (34)	51
46-65	3175/8637 (37)	502/1117 (45)	37
>65	1073/8637 (12)	238/1117 (21)	12
Race and ethnicity[b]			
Asian, non-Hispanic	428/8558 (5)	73/1106 (7)	5
Black or African American, non-Hispanic	1220/8558 (14)	197/1106 (18)	14
Hispanic, Latino, or Spanish	1473/8558 (17)	119/1106 (11)	17
White, non-Hispanic	5027/8558 (59)	685/1106 (62)	59
Multiracial/multiethnic	305/8558 (4)	26/1106 (2)	4
Other	105/8558 (1)	6/1106 (1)	1
Sex assigned at birth			
Female	6221/8602 (72)	711/1110 (64)	72
Male	2377/8602 (28)	399/1110 (36)	28
Intersex	4/8602 (<1)	0/1110	0
Vaccination status at index date[c]			
Unvaccinated	3291/8538 (39)	161/1095 (15)	16
Partially vaccinated	154/8538 (2)	21/1095 (2)	2
Fully vaccinated	4725/8538 (55)	860/1095 (79)	77
Date of last dose unknown	368/8538 (4)	53/1095 (5)	5
Cohort and prevalent SARS-CoV-2 strain at Index[d]			
Acute pre-Omicron	17/8646 (<1)	2/1118 (<1)	<1
Acute Omicron	2231/8646 (26)	388/1118 (35)	33
Postacute pre-Omicron	3732/8646 (43)	290/1118 (26)	28
Postacute Omicron	2666/8646 (31)	438/1118 (39)	39
Medically underserved area			
Yes	2369/8646 (27)	298/1118 (27)	28
No	6277/8646 (73)	820/1118 (73)	72
Rural participant			
Yes	465/8646 (5)	45/1118 (4)	4





Cameroni, Nature, 2021